

N O T I C E

THIS DOCUMENT HAS BEEN REPRODUCED FROM
MICROFICHE. ALTHOUGH IT IS RECOGNIZED THAT
CERTAIN PORTIONS ARE ILLEGIBLE, IT IS BEING RELEASED
IN THE INTEREST OF MAKING AVAILABLE AS MUCH
INFORMATION AS POSSIBLE


CR 167904

(NASA-CR-167904) EVALUATION OF LEFT
VENTRICULAR ASSIST DEVICE PUMP BLADDERS CAST
FROM ION-SPUTTERED POLYTETRAFLUORETHYLENE
MANDRELS (Thermo Electron Corp.) 103 p
HC A06/MF A01

N82-23976

Unclass
20238



 **Thermo
Electron**
CORPORATION

Report No. TE200-230-82

**EVALUATION OF
LEFT VENTRICULAR ASSIST DEVICE PUMP
BLADDERS CAST FROM ION-SPUTTERED
POLYTETRAFLUORETHYLENE MANDRELS**

March 1982

**Prepared for
NASA-Lewis Research Center
21,000 Brookpark Road
Cleveland, Ohio 44135**

**Prepared by
Thermo Electron Corporation
101 First Avenue
P.O. Box 459
Waltham, Massachusetts 02254**

TABLE OF CONTENTS

<u>Chapter</u>		<u>Page</u>
1	SUMMARY	1
2	STATEMENT OF WORK.....	3
	2.1 TASK I - MANDREL FABRICATION	3
	2.2 TASK II - MANDREL CLEANING AND INSPECTION	3
	2.3 TASK III - REMOVAL OF HIGH MOLECULAR WEIGHT SURFACE CONTAMINANTS FROM MANDRELS	4
	2.4 TASK IV - BLADDER FABRICATION.....	4
	2.5 TASK V - IN VIVO ION-SPUTTERED BLADDER IMPLANTATION AND EVALUATION.....	4
	2.6 TASK VI - IN VITRO BLADDER TESTS.....	5
	2.7 TASK VII - REPORTING	6
	2.7.1 NASA	6
	2.7.2 NHLBI	7
	2.8 TASK VIII - PRODUCT ASSURANCE REQUIREMENTS	7
3	RATIONALE	9
4	FABRICATION OF MICROTEXTURED MANDRELS	15
	4.1 ION THRUSTER TECHNOLOGY.....	16
	4.2 SPUTTER ETCHING OF PTFE MANDRELS	18
5	CHEMICAL	23
	5.1 CHARACTERIZATION OF ION-TEXTURED BLADDERS	23
6	ULTRASTRUCTURAL CHARACTERIZATION OF ION-SPUTTERED INTERFACES.....	77
7	IN VIVO STUDIES.....	83
8	IN VIVO RESULTS	87
	8.1 NASA LVAD NO. 2	92
	8.2 NASA LVAD NO. 3	95
	8.3 NASA LVAD NO. 1	95
	8.4 NASA LVAD NO. 4	96
9	DISCUSSION	99

1. SUMMARY

One of the most challenging requirements facing biomaterials is the development of a highly thromboresistant blood-contacting interface for use in implantable blood pumps. Biomaterials mechanics, dynamics, durability, surface morphology, and chemistry are among the critical considerations pertinent to the choice of an appropriate blood pump bladder material.

The use of transfer-cast biopolymers from ion-beam textured surfaces provides the opportunity to investigate subtle variations in blood pump surface morphology using Biomer as the biomaterial of choice. A cooperative program was established between Thermo Electron Corporation, NASA Lewis Research Center, and the Devices and Technology Branch (NIHLBI) to evaluate the efficacy of ion-beam sputtering as an acceptable method of fabricating textured blood interfaces.

Aortic grafts and left ventricular assist devices (LVAD's) were implanted in calves; the blood interfaces were fabricated by transfer casting methods from ion-beam textured polytetrafluoroethylene mandrels supplied by NASA-Lewis. The mandrels were textured by superimposing a 15- μ m screen mesh; ion-sputtering conditions were 300 volts beam energy, 40 to 50 mA beam, and a mandrel-to-source distance of 25 μ m. Under these conditions we obtained a microtextured surface composed of repeating pillar approximately 40 μ m in height, separated by a distance of 25 μ m.

A total of six in vivo experiments were carried out: two aortic grafts and four LVAD's. Chronologically, the aortic grafts were implanted at the outset of the study, since aortic grafts are technically less complex than cyclically pumping assist devices, and are thus less subject to post-operative complications. The surfaces of some of the prostheses were purposely coated with fibronectin preoperatively, in an effort to optimize fibroblastic adhesion; other prostheses were implanted without any surface modification, and were thus considered controls.

Our observations can be summarized as follows:

- Microtextured grafts and ventricular assist display thinner pseudoneointimal linings than conventionally textured surfaces.
- Fibronectinized surfaces produce biological linings containing larger amounts of collagen compared to linings obtained from control surfaces.
- The tested microtextured surface, composed of pillars $25\text{ }\mu\text{m} \times 25\text{ }\mu\text{m} \times 40\text{ }\mu\text{m}$ deep, resulted in poorly attached linings.
- The use of fibronectin increased lining adhesion, but the adhesion values are not considered adequate for trouble-free prostheses. Low lining adhesion may result in thromboembolic episodes.
- We thus conclude that ion-textured surfaces, as presently constituted, unsuitable as nonthromboembolic surfaces.
- We recommend that additional studies be carried out to optimize ion-textured surfaces designed for use in blood-contacting prostheses.

2. STATEMENT OF WORK

The Contractor shall provide all the necessary manpower, services, supplies, and equipment to perform the following tasks.

2.1 TASK I - MANDREL FABRICATION

The Contractor shall fabricate four (4) identical mandrels for transfer casting of left ventricular assist device bladders in accordance with the following requirements:

- A. Use polytetrafluoroethylene as the mandrel material having a known origin and processing history.
- B. Use standard calf left ventricular assist device bladder design to determine mandrel configuration.
- C. Fabricate four (4) identical mandrels using standard techniques.
- D. Inspect mandrels both macroscopically and microscopically for cracks and/or defects.
- E. Send mandrels to NASA-Lewis Research Center within 2 weeks after effective date of contract.

2.2 TASK II - MANDREL CLEANING AND INSPECTION

- A. Ultrasonically clean each mandrel in methylene chloride for 8 hours two separate times.
- B. Analyze an aliquot of the methylene chloride from the second sonification for contaminants by means of infrared spectroscopy.
- C. Repeat sonification until all soluble surface contaminants have been removed. No bladder will be fabricated from a mandrel until all soluble surface contaminants have been removed from the mandrel.

2.3 TASK III - REMOVAL OF HIGH MOLECULAR WEIGHT SURFACE CONTAMINANTS FROM MANDRELS

- A. Mechanically remove contaminants by casting a segmented polyurethane (BiomerTM) bladder on the mandrel and demold bladder.
- B. Using attenuated infrared spectroscopy, analyze inner bladder surface for fluorine, carbon, and other impurities.
- C. Repeat Task III.A and III.B until all foreign materials are mechanically removed.
- D. Perform Task III on each mandrel.
- E. Send to NASA Project Manager a section of demolded bladder from an ion-sputtered mandrel and a section of a bladder demolded from an untextured mandrel. The bladder shall be the one which was determined to be clean by the attenuated infrared.

2.4 TASK IV - BLADDER FABRICATION

- A. Fabricate ten (10) segmented polyurethane bladders using standard casting techniques.
 - 1. Five (5) bladders shall be made from the mandrel that has holes approximately 25 μm x 25 μm x 75 μm deep.
 - 2. Five (5) bladders shall be made from the mandrel that has holes approximately 25 μm x 25 μm x 40 μm deep.

2.5 TASK V - IN VIVO ION-SPUTTERED BLADDER IMPLANTATION AND EVALUATION

- A. Three (3) bladders of each design (total of six (6) bladders) shall be implanted along with the rest of the left ventricular assist device into calves.
- B. Previously established protocol for implantation, anticoagulation, and postoperative care shall be followed.

- C. After 30 days of pump operation, each implant shall be removed.
- D. Grossly examine the internal surface of each bladder upon explantation. Areas of interest shall include:
 - 1. Gross surface morphological composition.
 - 2. Continuity of thrombus/coagulum and pseudoendothelial deposition.
- E. Multiple photographs of gross specimens shall be taken.
- F. Divide bladder in half and put one half in a cold balanced electrolyte solution. The other half shall be fixed in buffered glutaraldehyde.
- G. Quantitatively determine the level of pseudointimal adhesion by measuring the peel strength in a high sensitivity Instron tester on rectangular 1 cm x 5 cm bladder samples.
- H. Measure thickness profiles on thin sections from the fixed specimens.
- I. Stain thin sections with eosin and measure cell density by light microscopy against a calibrated grid.
- J. Measurements shall be made on both longitudinal and circumferential specimens to define the pseudointimal composition.

2.6 TASK VI - IN VITRO BLADDER TESTS

- A. Use standard endurance test procedures to test pumping endurance capabilities of both bladder configurations cast from ion-sputtered mandrels.
- B. Test each bladder for a minimum of 10^6 cycles or until failure.
- C. After testing, examine each bladder for cracks and other failures.
- D. Photograph and document results of each bladder.

2.7 TASK VII - REPORTING

2.7.1 NASA

Reporting shall be in accordance with the Reports of Work attachment to this contract (excluding paragraphs A. and B.1.b) with the following exceptions:

- A. Within 10 days after effective date of contract, the Contractor shall submit in writing two (2) copies of a planned monthly expenditure schedule for the entire contract period with estimated times for and amounts of each expenditure. This schedule shall be in graph form with contract time in months as the abscissa and expenditures as the ordinate.
- B. Monthly Financial Reports shall be sent to:
 - 1. NASA Project Manager
 - 2. NASA Contracting Officer
 - 3. NASA-Lewis Research Center Audit Branch, MS 500-303

This report shall be in graphic form similar to the initial planned monthly expenditure schedule. The graph shall clearly display the costs during the reporting period and cumulative costs to date. Plotted on the same graph shall be the planned costs for the next reporting period.

- C. One copy of the Monthly Technical Progress Narrative shall be forwarded to the NASA Project Manager and one copy to the NASA Contracting Officer.
- D. The Final Report shall contain:
 - 1. Title: "Evaluation of Left Ventricular Assist Device Pump Bladders Cast From Ion-Sputtered Polytetrafluoroethylene Mandrels."
 - 2. NASA Contract Number.

3. A list of participating organizations in the overall evaluation.
4. NASA CR number.
5. Sponsoring agencies - NASA-Lewis Research Center and the National Heart, Lung, and Blood Institute.
6. Date.
7. The objectives, goals, progress, and results of each Task.

2.7.2 NHLBI

- A. A quarterly financial and technical progress report which describes the work performed during the prior 3-month period will be delivered to the Project Officer within 10 working days after the quarter being reported on. A comprehensive annual report, which will serve as a technical reference document describing all of the activities, significant scientific data, and presenting the results of the year's effort, will be delivered at the close of the contract.

2.8 TASK VIII - PRODUCT ASSURANCE REQUIREMENTS

- A. A continuous history of the fabrication, inspection, and test of the assist device bladders will be delivered with the bladders.
- B. The Contractor shall inspect and document those characteristics that materially influence the integrity and performance of the assist device bladders. Critical raw materials and parts shall be inspected and tested to determine conformance with existing specifications. Reports of actual test results shall be kept in the equipment log.

3. RATIONALE

In a related program, "Development and Evaluation of Textured Surfaces" (NO1-HV-3-2915), the effects of different mat thicknesses were being investigated with integrally textured bladders. To assess these effects, bladders were produced from master molds with surfaces of three fibril lengths, resulting in integral textures of three different mat thicknesses. However, the ability to produce reduced mat thicknesses was limited by the current method.

The basic postulate is that a lower mat thickness will result in a correspondingly reduced neointimal thickness. Years of experience with textured surfaces indicate that an initial coagulum is formed on the surface and covers any surface irregularity, until the coagulum forms a continuous blood interface. For example, when a textured surface of 300 μm is implanted in a calf, the initial coagulum will be at least 300 μm in thickness. It is expected that a textured surface of 100 μm would produce a thinner biologic lining compared to the above example, providing that similar hemodynamic parameters, anticoagulation regimen, and pumping conditions were in force. A thickness of 100 μm represents the lowest practical limit of the current methods. Therefore, the study of lower thicknesses requires different methodology.

From a strict, mechanical point of view, a thin neointima is desirable. Constant flexing introduces cyclic strains within the biologic lining, the strain ($\Delta L/L$), which increases with increasing thickness, reaches a maximum at the surface. To ensure long term flexure endurance of the neointimal lining, it would be advantageous to minimize surface strain. Thus, within practical limits a biologic lining should be as thin as possible.

Ion-beam texturing can produce regular surface roughnesses at a 10- μm pile height. A PTFE mandrel has been textured experimentally and bladders demolded from the mandrel. Figure 1 shows this texture at 100x and Figure 2 shows the same texture at 1000x. For comparison, conventionally

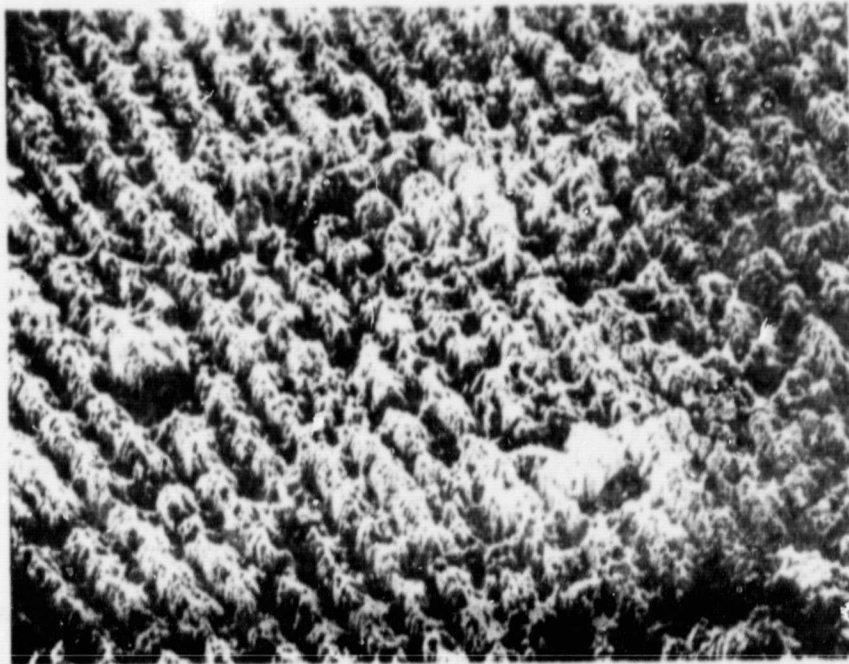


Figure 1. Integrally Textured Biomer Surface Obtained by Casting Against an Ion-Beam Textured PTFE Mandrel (100x)



Figure 2. High Power Photomicrograph of Surface in Figure 1 (1000x)

flocked and the present integrally textured surfaces are shown in Figures 3 and 4, respectively. Microsurfaces resulting from ion-beam texturing are expected to elicit thinner biologic linings than those obtainable by present methods, and are therefore seen as logical and desirable extensions of the present activities.

The intent of the present program was to elicit bladder surface mat thicknesses as thin as possible. However present methodology is a two-stage technique wherein the first stage requires a master mold which is electrostatically flocked with polyester fibrils. In the second stage, a silicone rubber mandrel is formed in this mold. During molding, fibrils are integrally cast into the surface of the mandrel. Following cure of the silicone rubber, the mandrel is removed from the master mold and the fibrils are dissolved from the mandrel surface. The resulting surface is a negative replica of the interior of the master mold with surface pores where the fibrils were originally. Bladders are fabricated by liquid casting techniques in which the bladder material is cast against the surface. When the bladder is demolded the interior (blood-contacting) surface is textured in a manner similar to that obtained by adhesively flocking the interior of conventional bladders. This method is limited by the size of the fibrils that are used for flocking the master mold. The length of these fibrils is controllable to a practical lower limit of approximately 250 μm , the smallest size being used in the current program.

In contrast to the current methodology, ion-beam texturing is a one-stage method of preparing mandrels. The texture is applied directly to the mandrel surface by ion bombardment and, after cleaning, the mandrel is ready for bladder fabrication. The bladder fabrication technique is identical to that currently used in producing integrally textured surfaces. The first coat is applied under a partial vacuum to ensure polymer filling of the pores in the mandrel surface. Additional coats are applied at ambient pressure until the desired bladder wall thickness is attained.

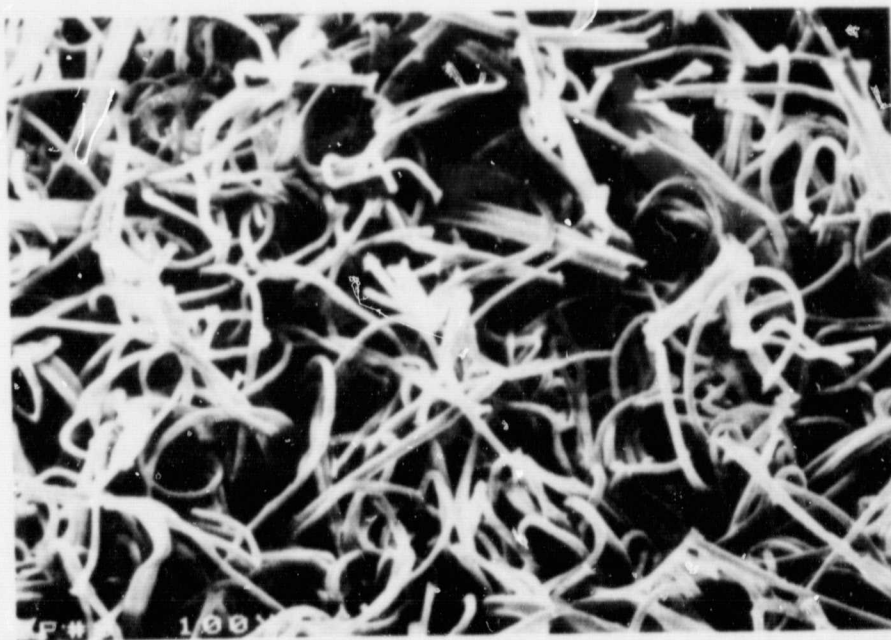


Figure 3. Integrally Textured Biomer Flock
Replica Surface (100x)

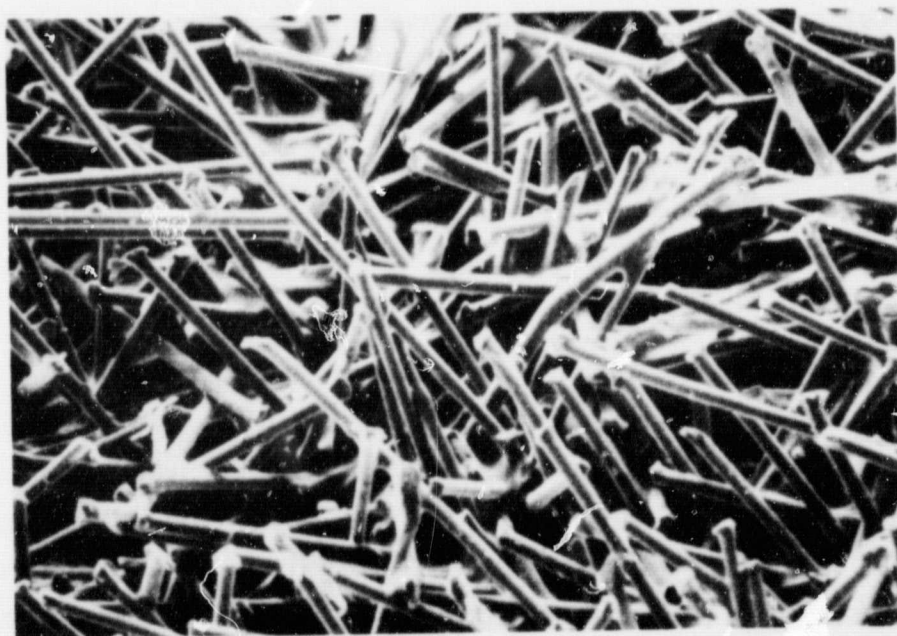


Figure 4. Conventionally Flocked Surface (100x)

We elected to assess this new blood interface in the Model 11 LVAD. This blood pump has been utilized in the current program for 5 years, and represents a well-characterized system, with little likelihood of encountering unexpected difficulties. Because engineering design, surgical approach, and animal maintenance will be identical to those currently used, the only variable being tested would be the new surface texture.



4. FABRICATION OF MICROTEXTURED MANDRELS

In 1975 the NASA-Lewis Research Center initiated a technology-specific spinoff program designed to more broadly utilize benefits resulting from ion thruster technology. An Ion-Beam Application Research (IBAR) program was organized to enable the development of new or improved materials, products, and processes through the nonpropulsive application of ion thruster technology.

In 1980 a cooperative program between Thermo Electron Corporation, the NASA-Lewis Research Center, and the Devices and Technology Branch of the National Heart, Lung, and Blood Institute, was initiated. The cooperative program was designed to determine the efficacy of ion-beam sputtering as an acceptable method of fabricating textured blood interfaces in LVAD's. The program was designed to be integrated with and compliment a related program "Development and Evaluation of Textured Surfaces" (NHLBI contract NO1-HV-3-2915), in which blood pump bladders were being molded on textured mandrels and subsequently evaluated in animal experiments. The NO1-HV-39-2915 study sought to determine the relationship between the effective mat thickness of integrally textured blood-contacting surfaces of cardiac assist devices and the resulting thickness and in vivo stability of the neointimal lining formed thereon.

Experience has shown that thin, uniform, and well-adhered pseudo-neointimal linings minimize the probability of thromboembolic complications, thereby greatly enhancing the suitability of devices for chronic operation. Techniques presently used to develop these integrally textured surfaces employ negative-replica casting, the master for which is prepared using conventional electrostatic discrete fiber blocking methods. Physical limitations on minimum flock fibril size limit the textured surfaces produced by this method to a minimum of approximately 100 μm . It is believed that optimum mat thickness may be considerably less than this currently obtainable value. The ion-beam method developed by NASA is capable of

producing microtextures resulting in mat thicknesses in the order of 10 μm , an order of magnitude smaller than otherwise achievable. Thus, it was our hypothesis that such finely textured surfaces would produce very thin, stable pseudoneointimal linings with correspondingly improved chronic device performance.

The current program extended and complemented the effort already underway on NO1-HV-3-2915, to include the in vivo evaluation of two additional mat thicknesses, nominally 40 μm and 75 μm in depth. The effort was carried out using identical methods of performance evaluation employed on NO1-HV-3-2915, thereby affording direct comparison of results.

As demonstrated by existing methods of texturing surfaces autologously derived biological linings are formed by the deposition of circulating blood components. It was anticipated that similar linings would form on microtextured bladders fabricated on ion-sputtered mandrels. Because of the significantly finer texture, we expected the resultant linings to be thinner than anything previously attained. It was also reasonable that biochemical and cytological composition be comparable, although the degree of lining adhesion was expected to be less than that obtained with coarser texture, due to the reduction in effective bonding area.

This program was intended to demonstrate the feasibility of a new texturing approach, without any optimization, and therefore our results must be considered to be preliminary rather than conclusive. If these preliminary experiments show a significant reduction in pseudoneointimal lining thicknesses, improvements in the degree of adhesion may be contemplated using current techniques or modifications thereof.

4.1 ION THRUSTER TECHNOLOGY

Figure 5 shows a schematic drawing of an operating electron bombardment ion thruster system. As can be seen, the electron-bombardment ion thruster is a low-pressure gaseous discharge device, and thus can operate only in a vacuum environment. The propellant, shown as mercury

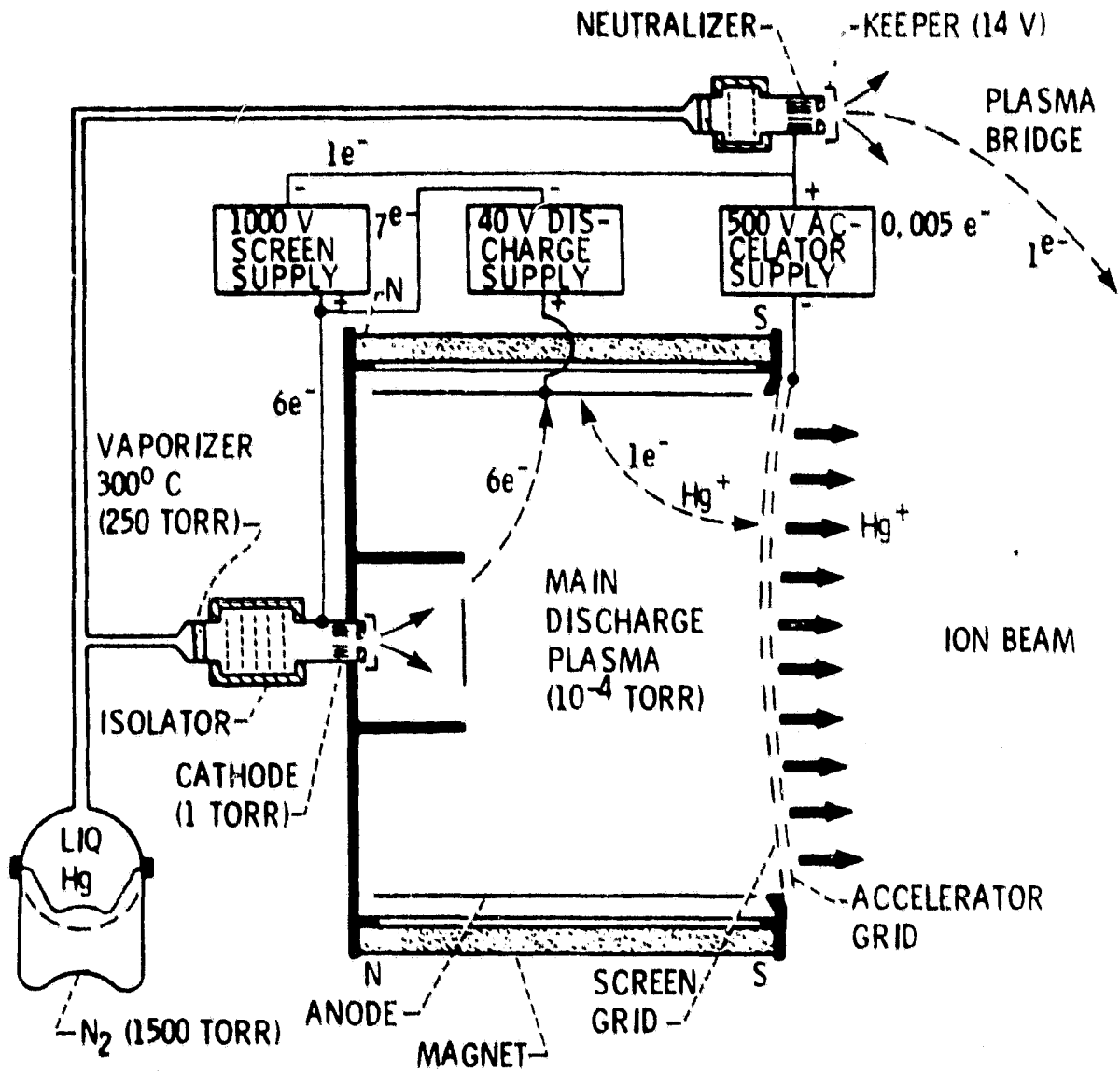


Figure 5. Electron Bombardment Ion Thruster System Schematic

in Figure 5, can be any liquid or gas capable of being easily vaporized and ionized. Other propellants such as cesium, hydrogen, argon, and xenon have been frequently used. The propellant is vaporized and fed into a discharge chamber where it is ionized by electron bombardment. An axially diverging magnetic field is used to increase the path length, and thereby the ionization efficiency, of electrons leaving the cathode toward the anode. Thrust is produced as a result of electrostatic acceleration of ions under the influence of the high electric field between the screen and accelerator grids. The exhaust ions have energies equal to the voltage of the screen supply, typically between 200 and 2000 eV. Electrons are added to the exhaust ion beam to maintain charge neutralization of the ion beam and to prevent an accumulation of electrons on the machine.

In our application, we utilized the resulting ion beam to sputter etch a polytetrafluoroethylene (PTFE) mandrel placed downstream of the ion source, by a method known as sputter etching. This method will be fully discussed in the following section.

4.2 SPUTTER ETCHING OF PTFE MANDRELS

Sputter etching is the removal of material from a surface by energetic ion or neutral particle bombardment. The bombarding particles interact with the surface through collision processes so as to cause the ejection of surface atoms, molecules, or molecular fragments. Figure 6 depicts an ion source used for sputter etching a target that is partially protected by a sputter mask. The sputter mask material also is sputter etched and is typically chosen of a material more sputter resistant than the target (in our case we utilized a copper microscreen).

The sputter etch rate of materials is dependent to varying degrees upon the following parameters:

- Bombarding species
- Target material

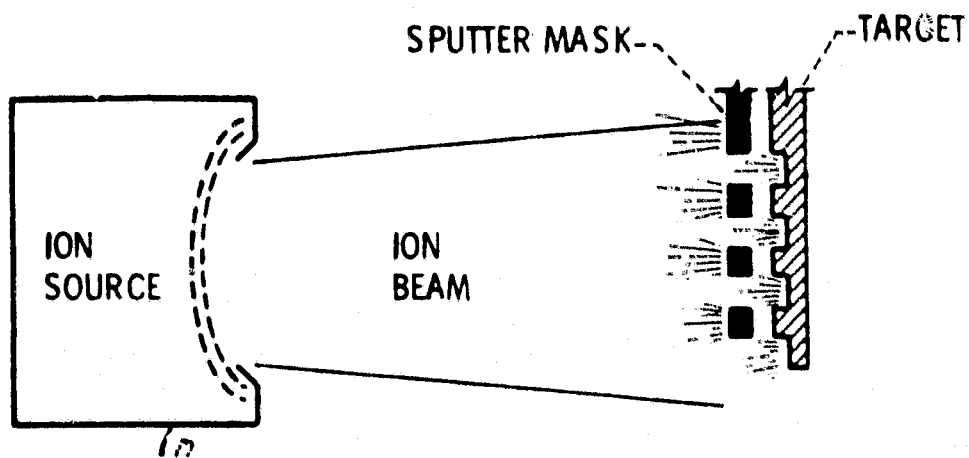
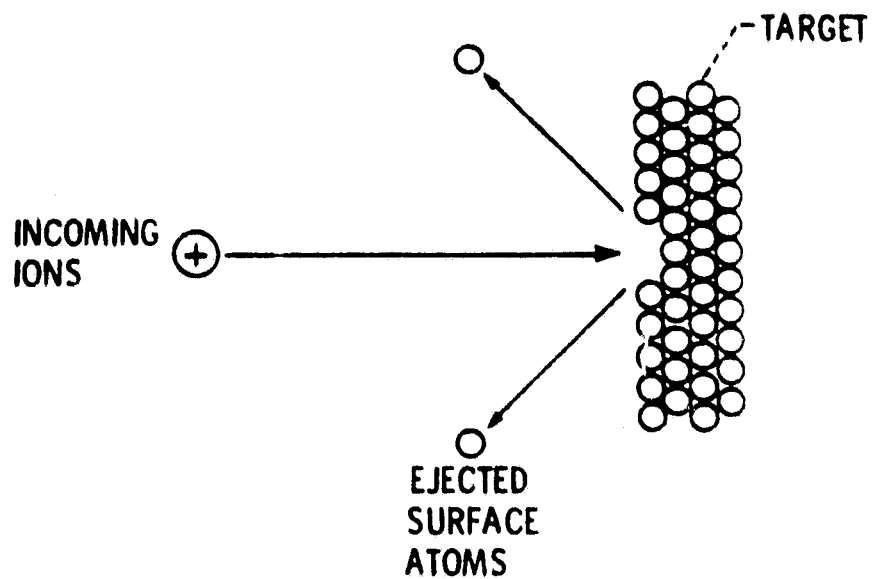


Figure 6. Ion Beam Sputter Etching a Target Partially Protected by a Sputter Mask

- Energy of the bombarding species
- Current density of the incident ion beam
- Angle of incidence with respect to the target surface
- Background environmental gas pressure and composition
- Target temperature (which may also be influenced by the ion beam power density)
- Target purity and composition of impurities
- Target crystallographic structure and orientation of crystalline planes

We decided to utilize PTFE for two reasons. One, PTFE polymers can be efficiently sputtered at a rate of $6.2 \times 10^4 \text{ } \overset{\circ}{\text{A}}/\text{min}$ when bombarded by 500-EV argon ions at a current density of 1 mA/cm^2 . This sputtering rate permits relatively fast production of microtextured mandrels. The second reason is that PTFE mandrels permit easy demolding of polyurethane films, due to the material's inherent nonstick surface characteristics.

Figure 7 presents the sputter etching technique utilized in this program to produce a uniformly repeating pitted surface on PTFE mandrels. The ion-sputtered mandrels are subsequently utilized in the fabrication of aortic grafts and Model 11S LVAD's, by solution casting films of a segmented polyurethane (Biomer).

The application of ion-beam sputtering techniques using PTFE mandrels allows fabrication of cardiovascular devices having surface micro features in the 1- to 300- μm range. The heights of the resulting surface pillars are simply dependent upon the duration, current density, and ion energy used for the mandrel sputtering.

We planned to produce and evaluate two different microtextured heights: $25 \mu\text{m} \times 25 \mu\text{m} \times 40 \mu\text{m}$ in depth, and $25 \mu\text{m} \times 25 \mu\text{m} \times 75 \mu\text{m}$ deep. Because of the shortness of the program (1 year) we only received from NASA-Lewis mandrels textured to $25 \mu\text{m} \times 25 \mu\text{m} \times 40 \mu\text{m}$. Therefore, all of our in vivo studies were conducted with aortic grafts and LVAD's fabricated from these mandrels. The deeper microtextures (75 μm in depth) were not manufactured, and thus could not be evaluated.

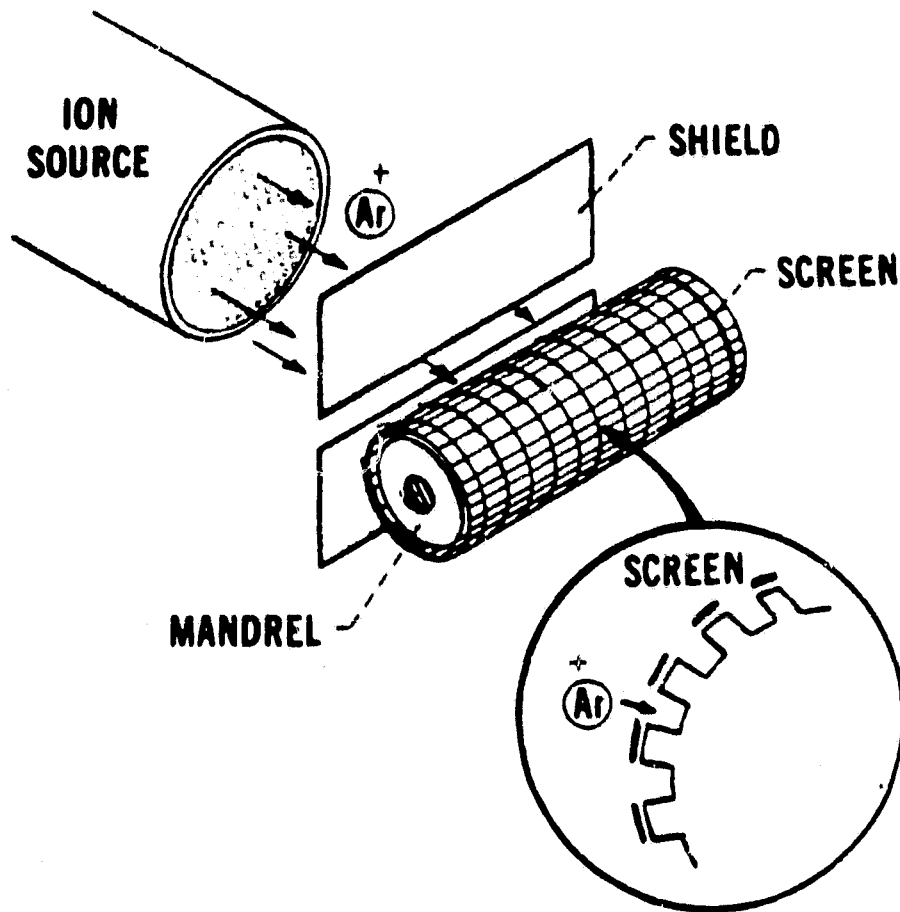


Figure 7. Sputter Etching Technique to Produce Pits on a Polytetrafluoroethylene Mandrel by Sputtering Through an Electroformed Mesh Screen

5. CHEMICAL

5.1 CHARACTERIZATION OF ION-TEXTURED BLADDERS

Aortic grafts and Model 11S LVAD's were fabricated by successively immersing the ion-sputtered PTFE mandrels into a low-viscosity Biomer solution. The apparatus used for this purpose is shown in Figure 8.

The selected method of fabricating Biomer bladders from ion-beam microtextured negative replica PTFE mandrels is a novel approach. It represents a key concept which is envisioned to bypass hitherto troublesome aspects of ion-texturing technology - namely unavoidable polymer degradation. Localized surface heating of polymers can cause melting, chain scission, evaporation, and crosslinking. Thermal evaporation of PTFE causes decomposition involving formation of free radicals due to random polymer chain scission. The results of several investigators indicate that thermal decomposition of PTFE in the range of 360° to 600°C results in formation of C_2F_4 (Tetra Fluoro Ethene) as the primary product. The latter group of investigators performed RF decomposition of PTFE at 11.5 torr, resulting in a distribution of products shown in Table 1.

Most of these reaction products can be expected to evaporate during processing, but some amount will condense on the cold polymer, and thus constitute a potential source of blood contamination. To purify the textured mandrel from the surface contaminants we decided to twice ultrasonicate the PTFE in methylene chloride for periods of 8 hours each. The first sonication was expected to dissolve a significant fraction of the aforementioned contaminants, while the second sonication is undertaken as an added insurance measure. As a precautionary measure, an aliquot of methylene chloride from the second sonication was assayed for contaminants by means of infrared spectroscopy. A PTFE mandrel was not released for fabrication until all soluble surface contaminants have been removed.

At pressures of approximately 2×10^{-3} torr, other researchers have performed RF sputtering of PTFE with inert gases, resulting in deposition

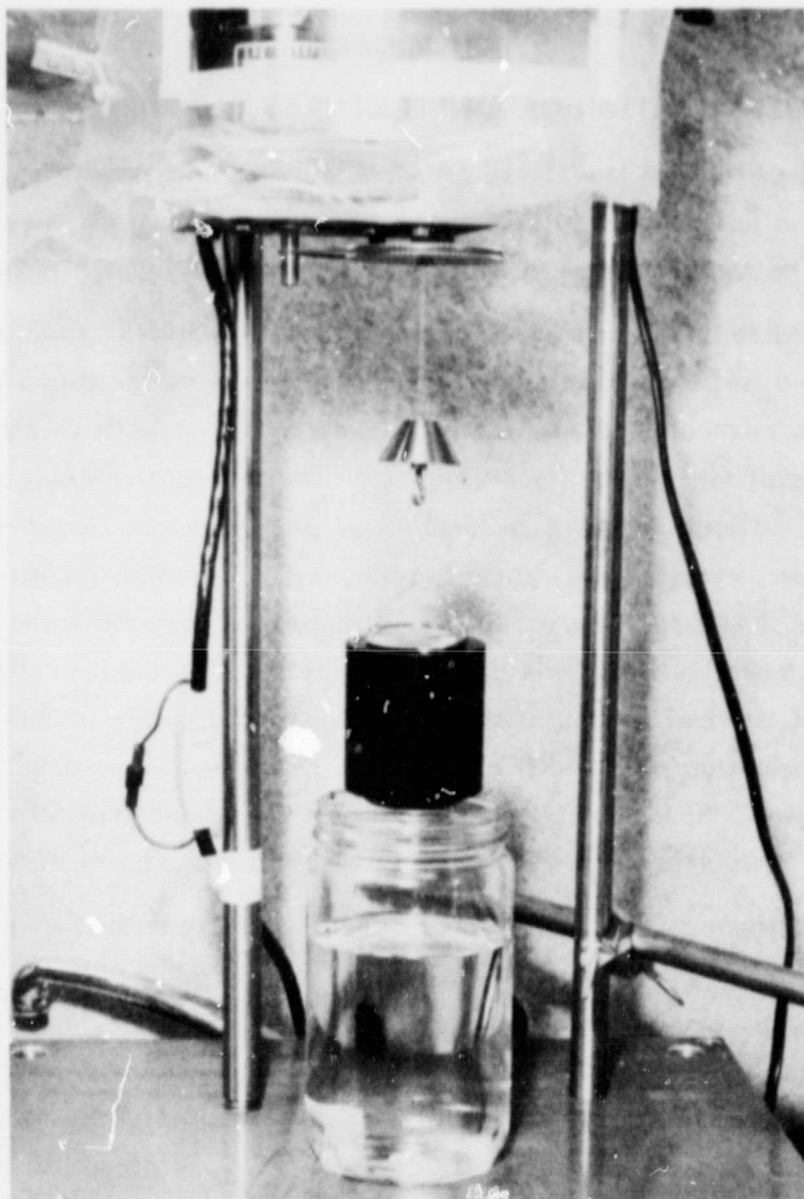


Figure 8. Apparatus for Sequential Dipping of Mandrels Textured by Ion-Sputtering Techniques

TABLE 1
REACTION PRODUCTS OF RF PTFE DECOMPOSITION

Product	Structural Formula	Distribution
Tetrafluoro Methane	$\begin{array}{c} \text{F} \\ \\ \text{F}-\text{C}-\text{F} \\ \\ \text{F} \end{array}$	0.37
Hexafluoro Ethane	$\begin{array}{c} \text{F} \quad \text{F} \\ \quad \\ \text{F}-\text{C}-\text{C}-\text{F} \\ \quad \\ \text{F} \quad \text{F} \end{array}$	6.43
Tetrafluoro Ethene	$\begin{array}{c} \text{F} \quad \text{F} \\ \quad \\ \text{F}-\text{C}=\text{C}-\text{F} \end{array}$	85.22
Hexafluoro Propene	$\begin{array}{c} \text{F} \quad \text{F} \quad \text{F} \\ \quad \quad \\ \text{F}-\text{C}=\text{C}-\text{C}-\text{F} \\ \quad \quad \\ \quad \quad \text{F} \end{array}$	5.90
Octafluoro Propane	$\begin{array}{c} \text{F} \quad \text{F} \quad \text{F} \\ \quad \quad \\ \text{F}-\text{C}-\text{C}-\text{C}-\text{F} \\ \quad \quad \\ \text{F} \quad \text{F} \quad \text{F} \end{array}$	2.08

of yellow-colored polymers. These polymers are crosslinked versions of linear PTFE. The mechanism of polymerization has been described, and involves intermediate radical and monomer ion formation as a result of the plasma's ion bombardment. The surface species continually react to form extensive crosslinking and unsaturation resulting in high mechanical strength fluoropolymer films. Fluorine deficiency in the form of free or incompletely bonded carbon causes strong adsorption of blue light resulting in a yellowish appearance when viewed in white light. Our experience indicates that some surface crosslinking does indeed take place, as evidenced by a yellow tone of a PTFE test mandrel textured at NASA-Lewis in support of this proposal. From our standpoint, this crosslinking is advantageous during Biomer bladder demolding. Crosslinking tends to increase surface hardness, facilitating bladder removal. This was confirmed during preliminary trials where Biomer films were easily removed from textured PTFE mandrels.

Although we were reasonably convinced that low molecular weight contaminants will be removed during sonication, higher molecular weight fragments, insoluble in methylene chloride, could remain on the mandrel surface. High molecular weight contaminants were removed mechanically; several films were cast on the mandrel and demolded; contaminants who adhere to the film and would remove as the films are demolded. For this reason, we produced several sacrificial bladders. The inner surfaces of these bladders were scanned by Electron Spectroscopy for Chemical Analysis (ESCA) in search of fluorine, carbon, and other impurities. Only after we were reasonably convinced that all foreign materials were mechanically scrubbed, did actual bladder fabrication begin. Although direct ion sputtering of PTFE decomposes the surface, all contaminants were removed prior to bladder fabrication, thus ensuring purity and reproducibility of the blood-contacting interface.

We submitted nine polymer specimens to Structure Probe Inc. for ESCA analysis. The purpose of this surface analysis was to compare the elemental and chemical composition of the polymers, with particular attention to the presence of nickel on the demolded Biomer films. Nickel is a potent biocide; traces of this metal could contaminate the surface of demolded Biomer bladders, originating from the nickel screen used in the ion-sputtering process. It was important to ascertain how many demoldings were necessary to completely clear the surface of the ion-sputtered PTFE mandrel of any traces of nickel.

For this purpose we selected the case of ESCA techniques; this ultra-sensitive surface technique is capable of detecting nanogram quantities of nickel, to a depth of 50 Å. The excitation source in ESCA is an x-ray beam of predominantly Mg K α x-rays. The x-rays have enough energy to knock out electrons from orbital shells of atoms in the sample. Electrons from atoms within the top 20 Å of the surface have enough energy to escape and are available for detection as photoelectrons with an energy equal to the difference between the Mg K α energy and the orbital shell binding energy. The ESCA spectra are plotted with binding energy on the horizontal axis and electron intensity on the vertical axis.

Reference to the attached table of ESCA Photoelectron Binding Energies allows elemental identification by merely comparing the measured electron peak energy to the tabulated values. As with Auger spectroscopy, all elements except H and He can be detected. In addition, however, ESCA can measure the photoelectron binding energy so precisely that shifts in energy due to changes in chemical bonding can be studied resulting in complete information about chemical compounds present in the analyzed layer. The following table presents the Estimated Atomic Composition of the samples tested. Figures 9 through 56 present the ESCA fingerprints obtained from these specimens.

ESTIMATED ATOMIC COMPOSITIONS (%)

Sample	C	O	F	Si	N	Ni	Cl
PTFE Rod (Control)	35.1	1.8	63.2	-	-	-	-
PTFE Mandrel	44.2	4.8	46.4	4.7	-	-	-
Biomer Control	58.8	22.1	-	18.1	1.1	-	-
Demolding No. 1	55.9	20.8	9.9	12.1	1.2	0.1	-
Demolding No. 2	64.9	20.5	-	14.2	-	0.3	-
Demolding No. 3	63.7	22.1	1.1	11.4	1.3	0.3	-
Demolding No. 4	71.1	18.0	0.6	9.5	0.8	-	-
Demolding No. 5	58.7	18.5	7.7	12.9	2.2	-	-
Fibronectinized Biomer	68.8	17.5	-	10.6	1.6	-	1.6

As the table indicates, a virgin PTFE rod (control) is composed primarily of carbon and fluorine, with a small amount of dissolved oxygen at the surface. An ion-textured PTFE mandrel, after five sacrificial demoldings, contains primarily carbon and fluorine, with small amounts of oxygen and silicone at the surface; the silicone appears to originate from the Biomer solution.

Biomer control is a sheet of Biomer cast on glass; like any polyurethane polymer, Biomer is composed of carbon, oxygen, and nitrogen with a surprisingly large concentration of silicone. This level of silicone can not be a contaminate; it is possible that a silicone polymer is added to Biomer as an additive. Demoldings 1 through 5 are sacrificial Biomer bladders cast on ion-sputtered PTFE mandrels; as the table indicates, the first three sacrificial demoldings contain nickel as a contaminant, but after four demoldings the surface of the PTFE has been sufficiently cleared to be considered ready for the production of implantable bladders. As a curiosity, we also included a specimen of a fibronectinized Biomer bladder; in this case a small amount of chlorine is observable on the surface. The chlorine originates from the buffer used in the fibronectin solution.

In conclusion, ion-sputtered PTFE mandrels can be cleaned of surface nickel impurities after two sonications of methylene chloride and a minimum of three sacrificial demoldings. Under these conditions, these mandrels were deemed ready for use in the fibronectin of cardiovascular devices.

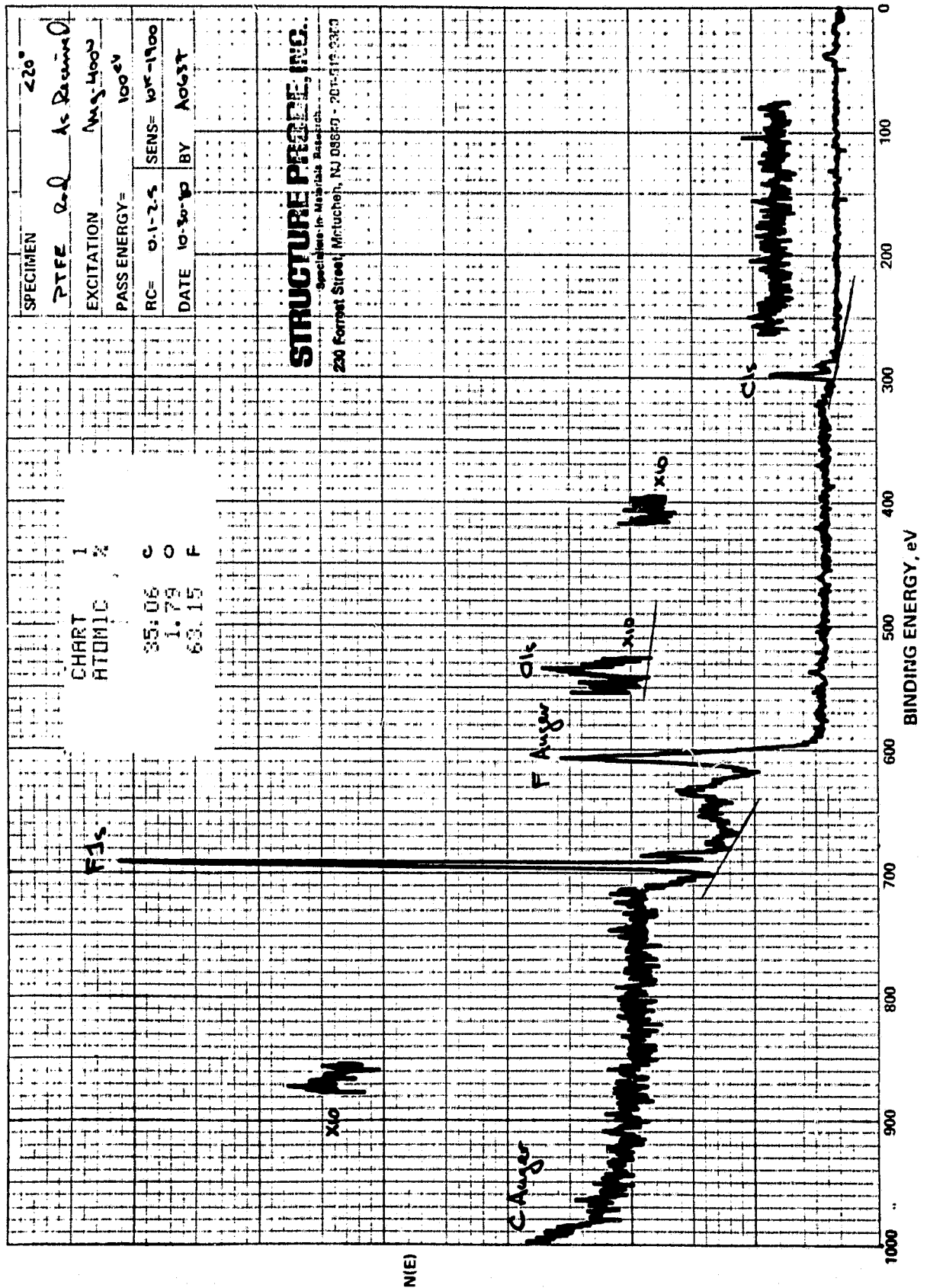
ORIGINAL PAGE IS
OF POOR QUALITY


Figure 9



PHYSICAL ELECTRONICS INDUSTRIES, INC.
174020

ORIGINAL PAGE IS
OF POOR QUALITY

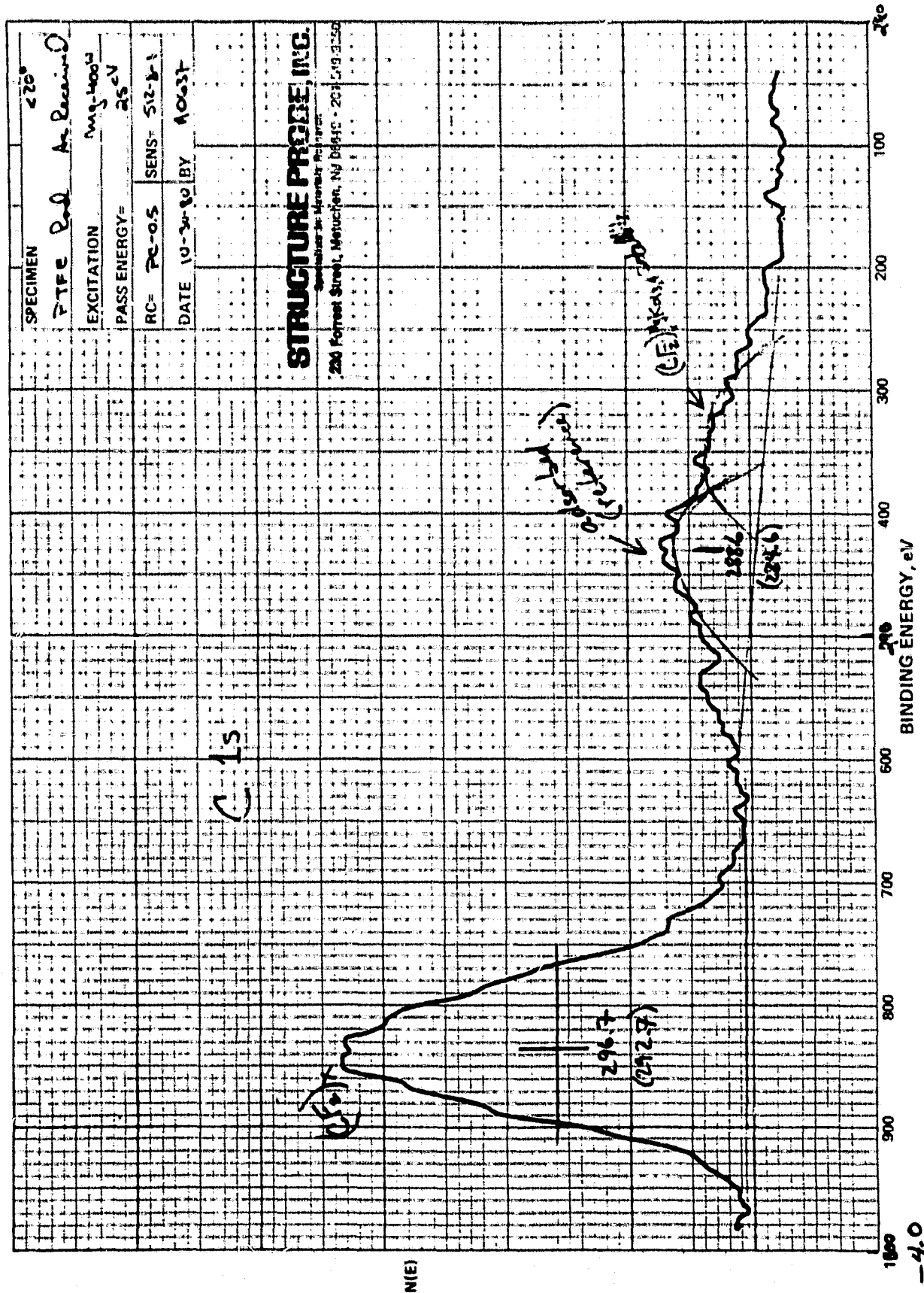


Figure 10

A-6351

ORIGINAL PAGE IS
OF POOR QUALITY

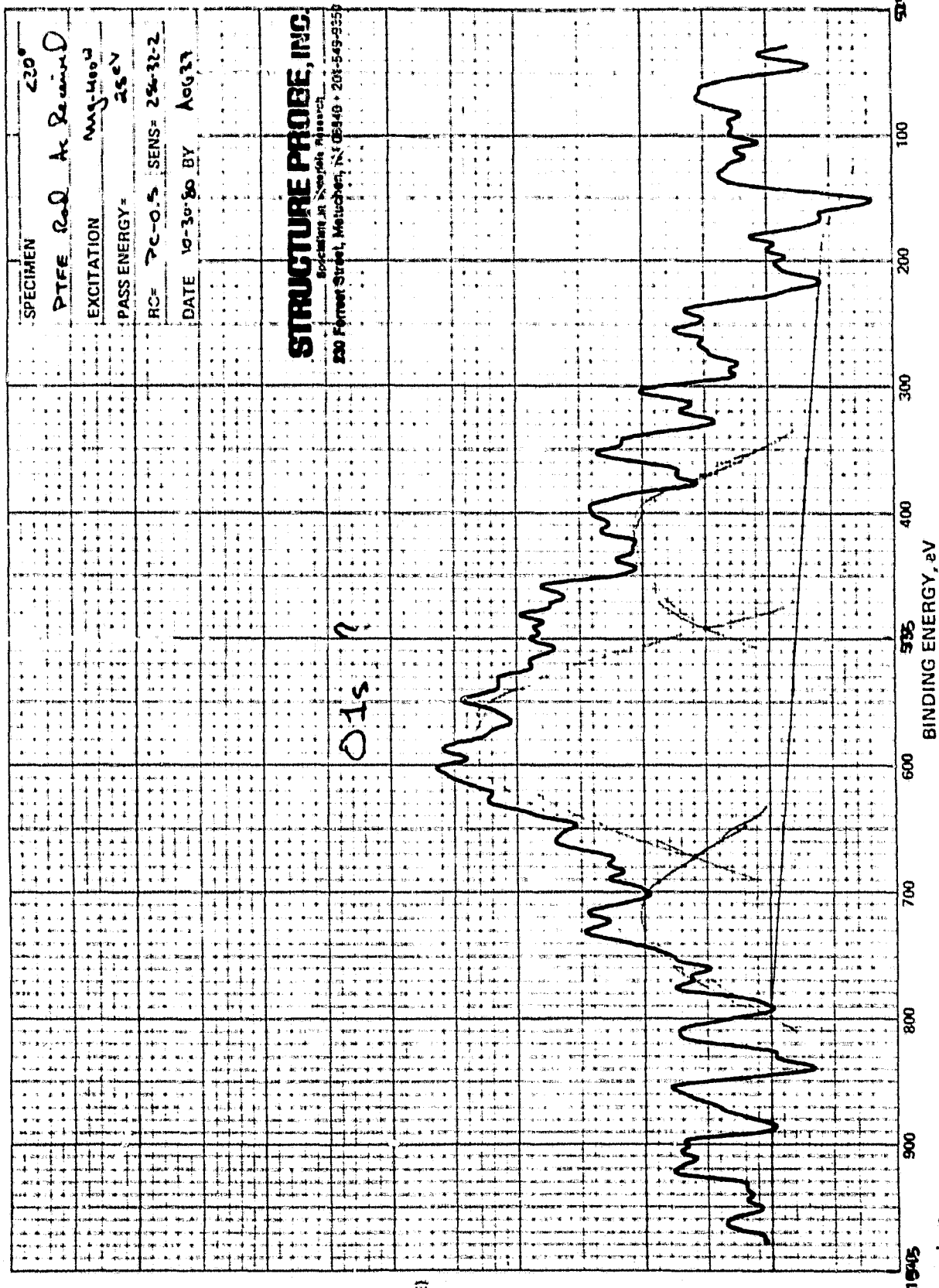


Figure 11

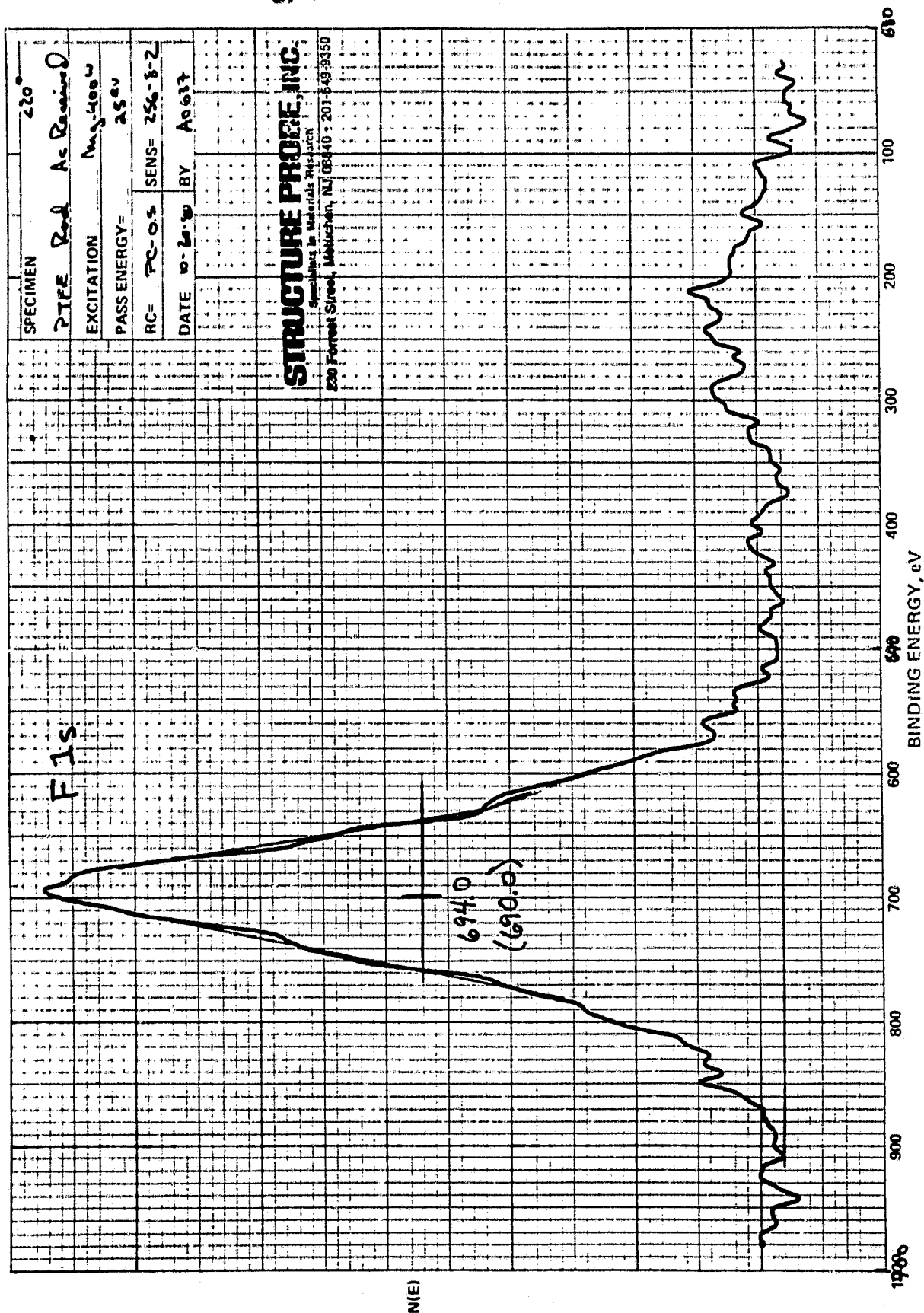
ORIGINAL PAGE IS
OF POOR QUALITY


Figure 12

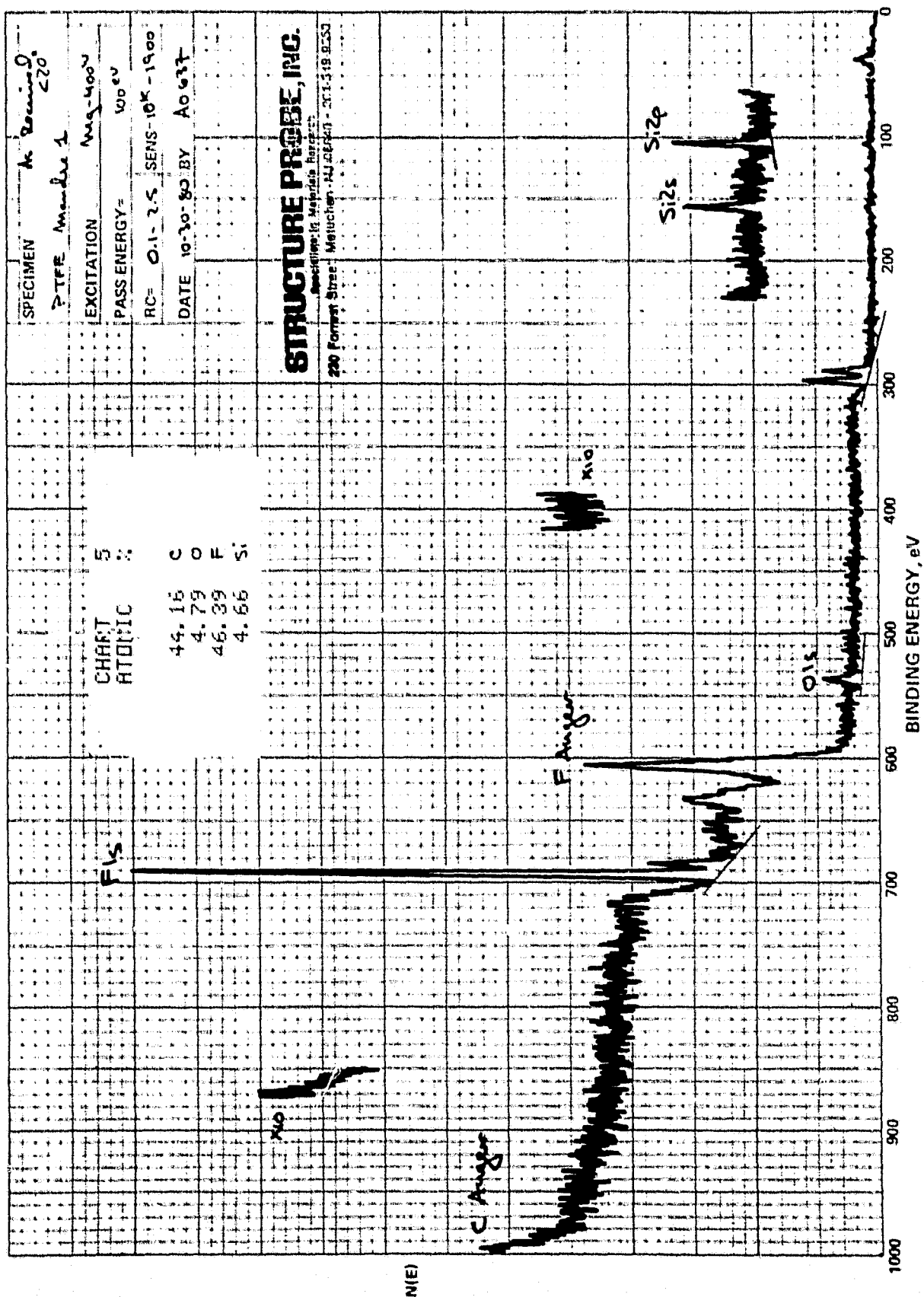
ORIGINAL PAGE IS
OF POOR QUALITY


Figure 13

ORIGINAL PAGE IS
OF POOR QUALITY

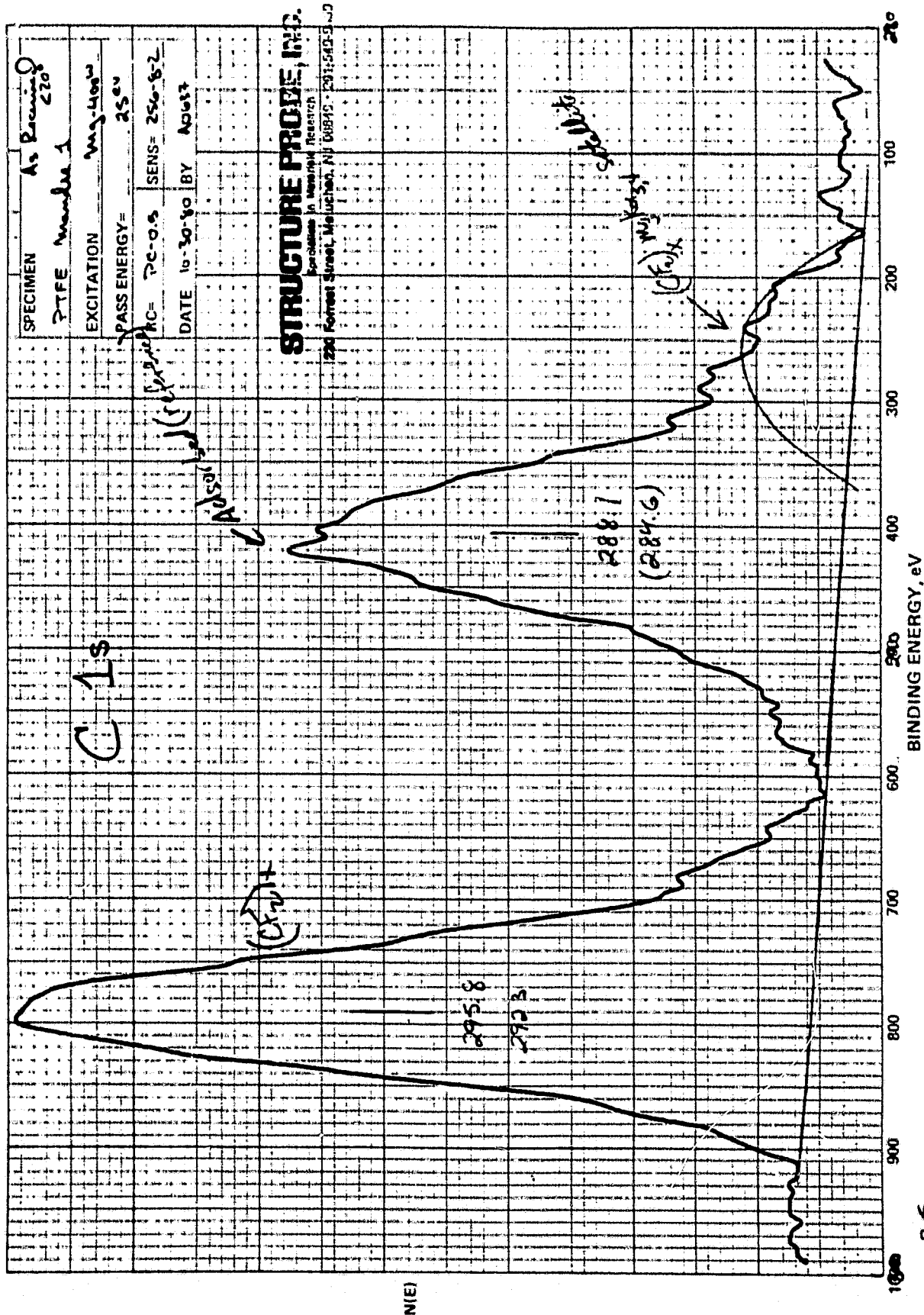


Figure 14

ORIGINAL PAGE IS
OF POOR QUALITY

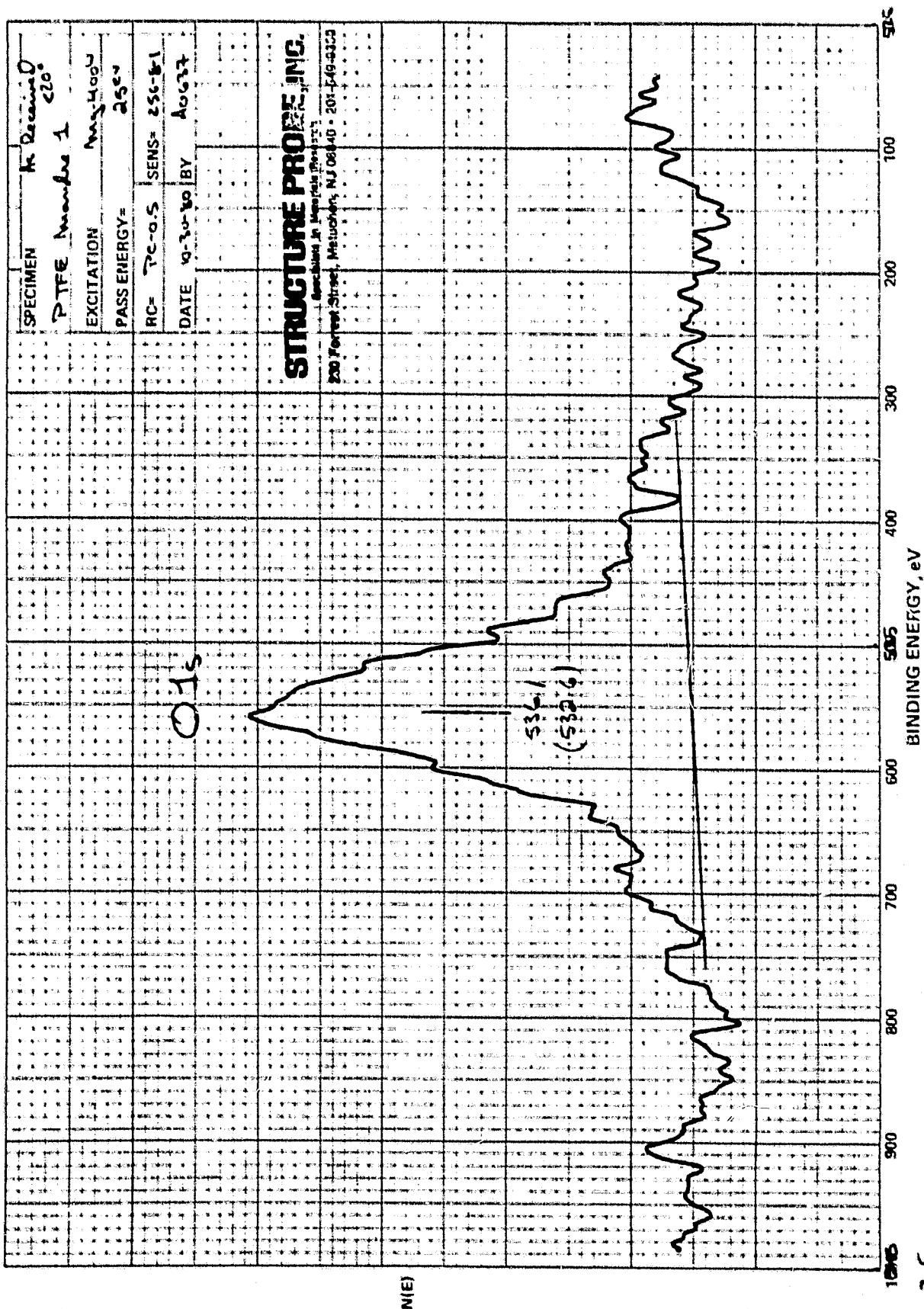


Figure 15

Figure 16

ORIGINAL PAGE IS
OF POOR QUALITY

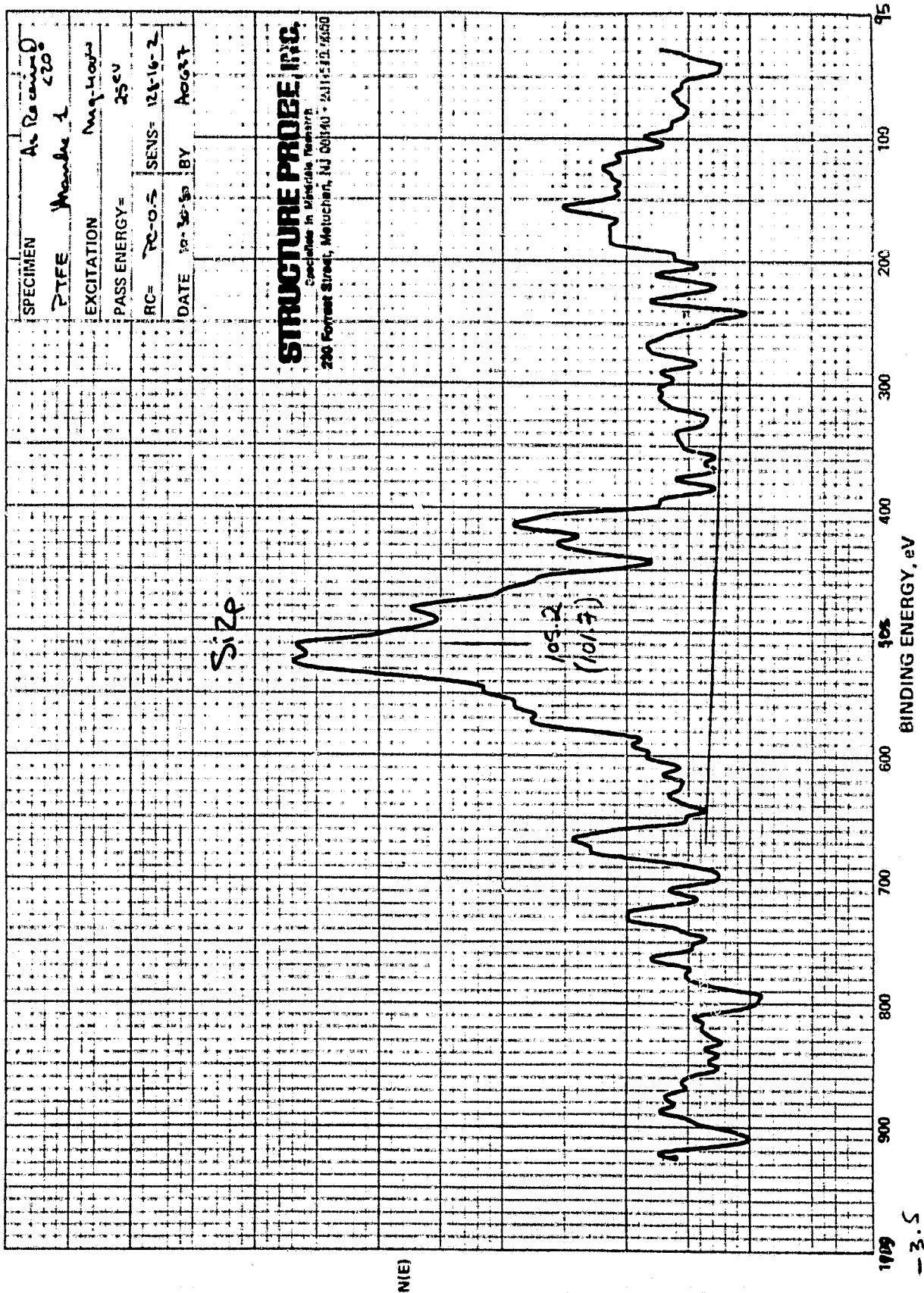


Figure 17

ORIGINAL PAGE IS
OF POOR QUALITY

A-6358

PHYSICAL ELECTRONICS INDUSTRIES, INC.
174020

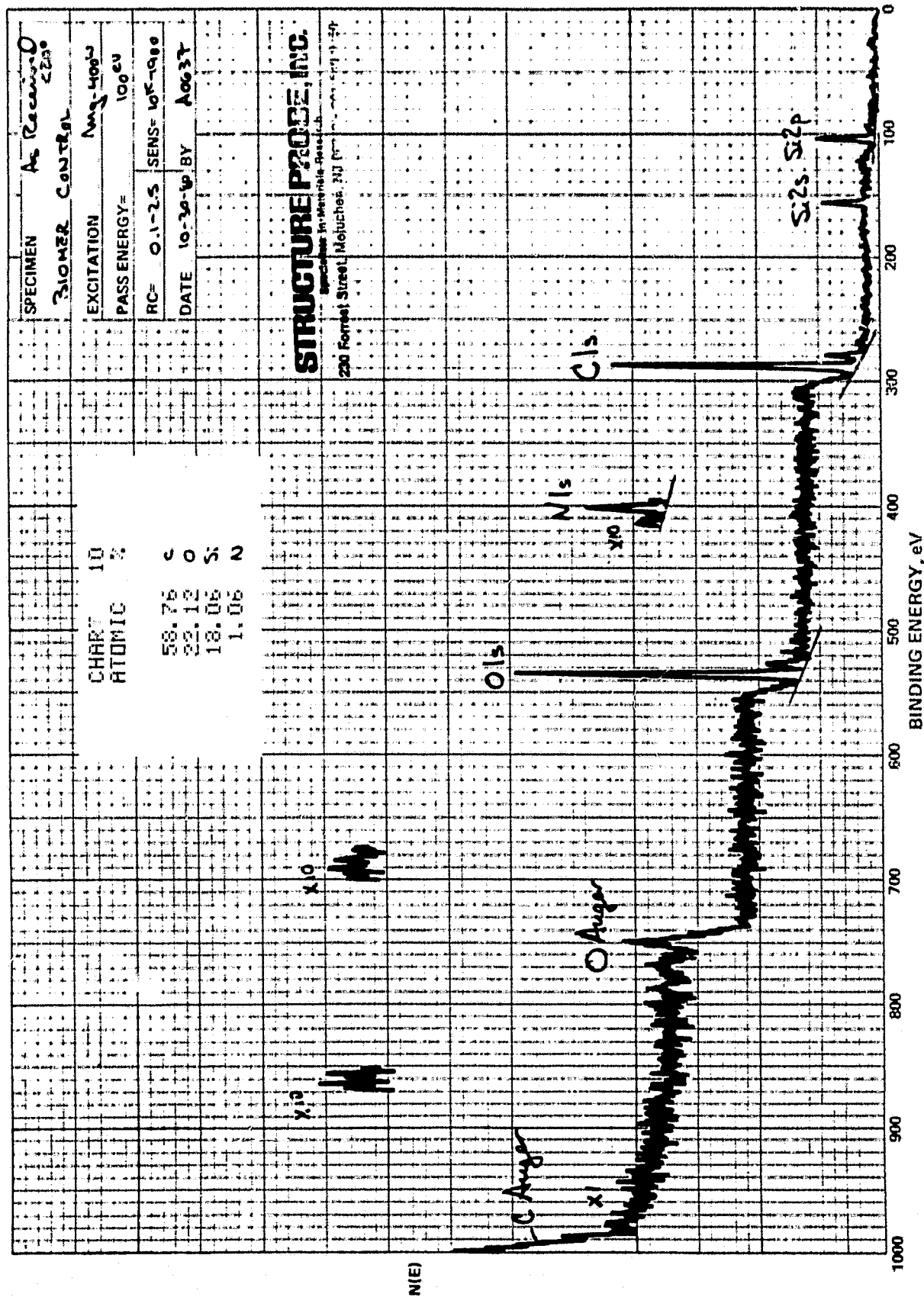


Figure 18

ORIGINAL PAGE IS
OF POOR QUALITY

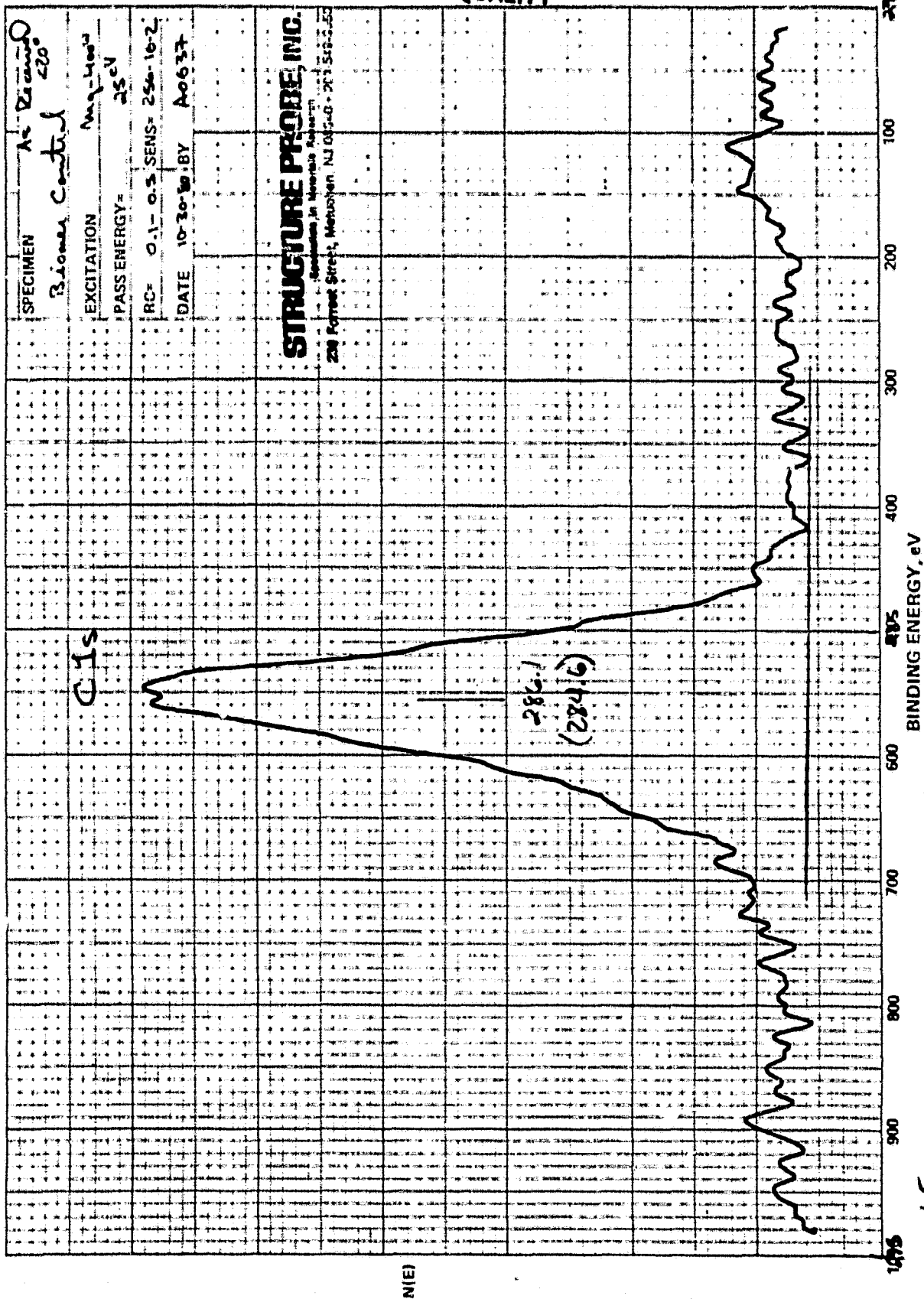


Figure 19



PHYSICAL ELECTRONICS INDUSTRIES, INC.
174020

A-6360

ORIGINAL PAGE IS
OF POOR QUALITY

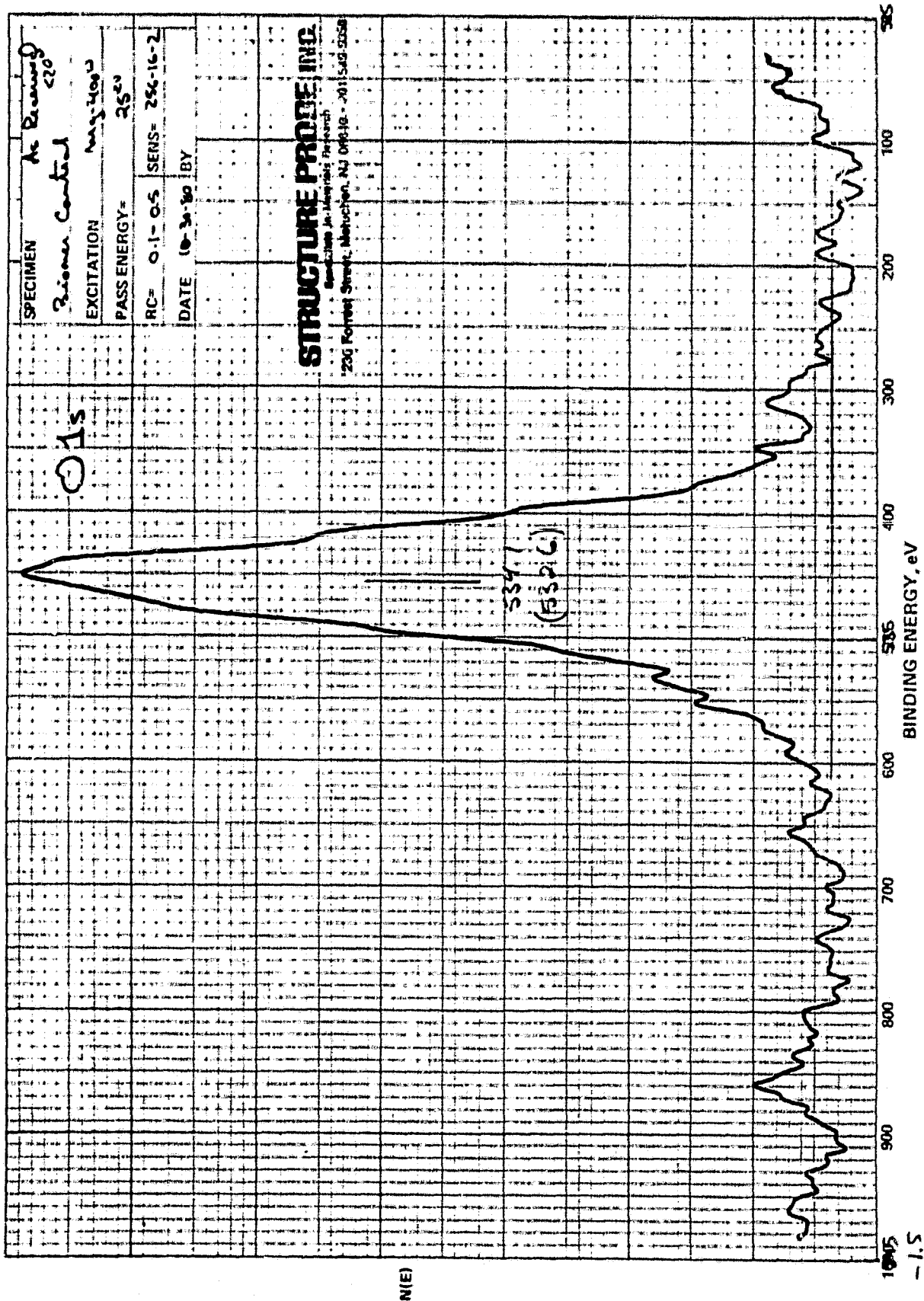


Figure 20

A-6361

PHYSICAL ELECTRONICS INDUSTRIES, INC.
174020

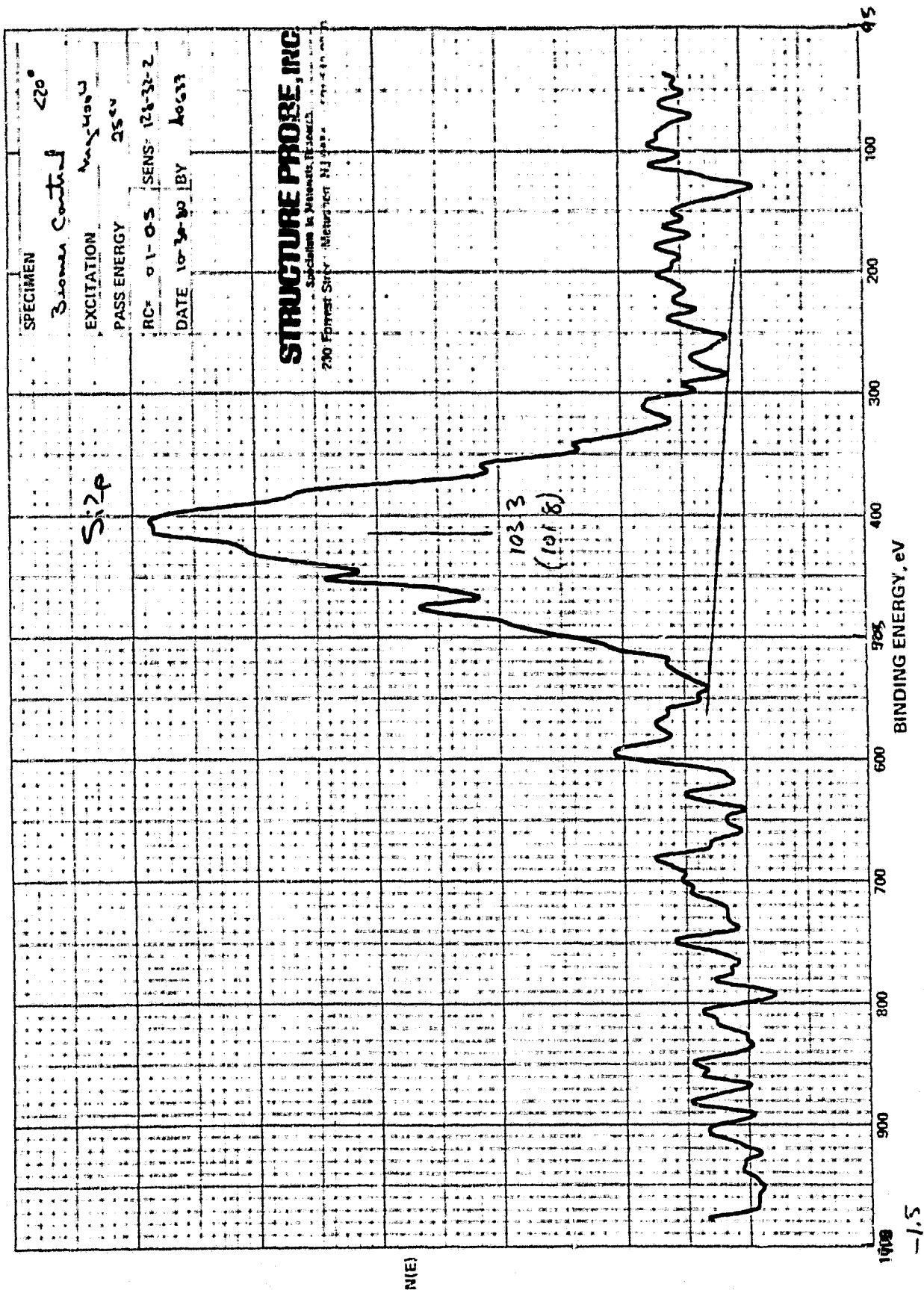


Figure 21

A-6362



ORIGINAL PAGE IS
OF POOR QUALITY

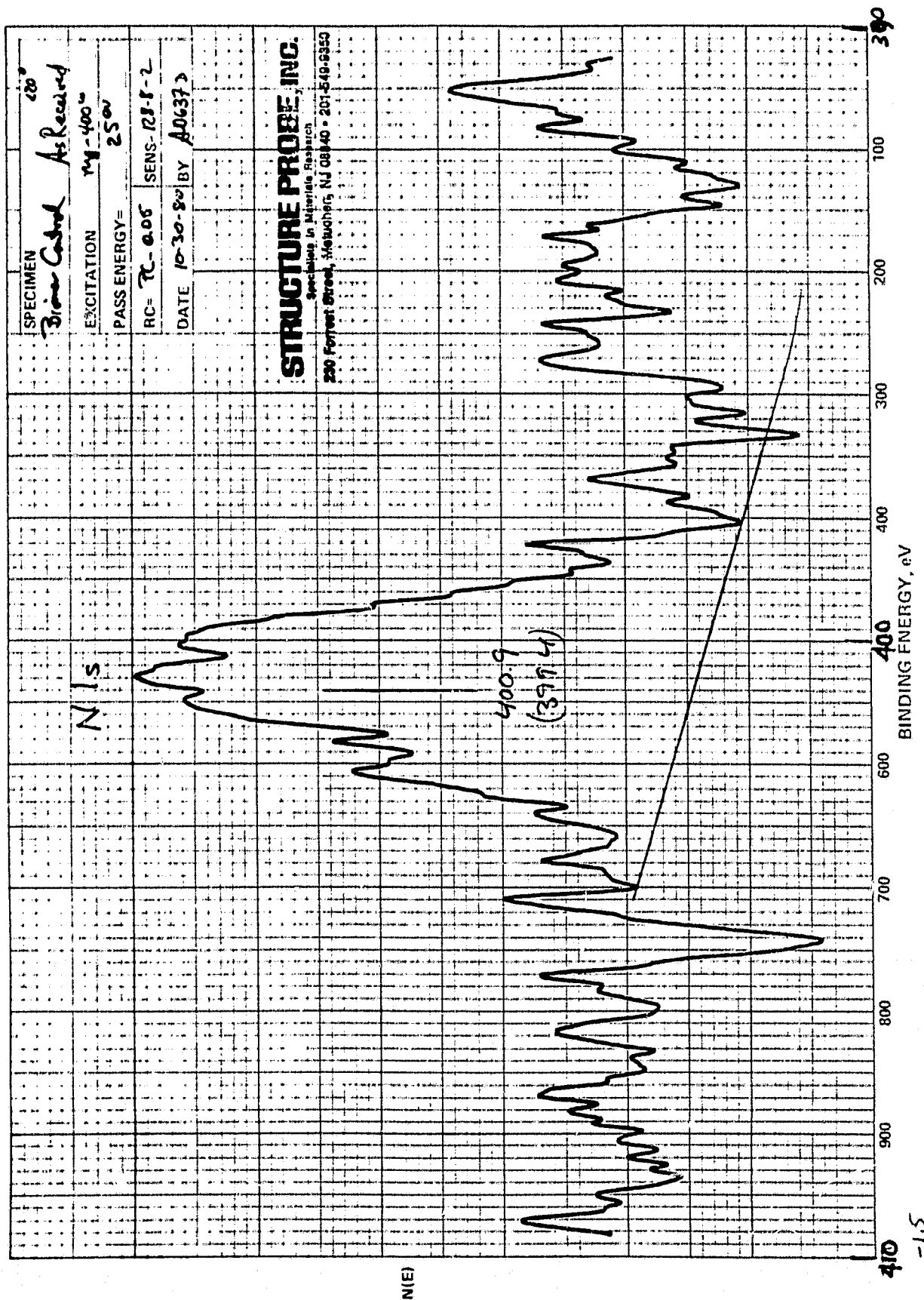


Figure 22

A-6363

PHYSICAL ELECTRONICS INDUSTRIES, INC.
174020

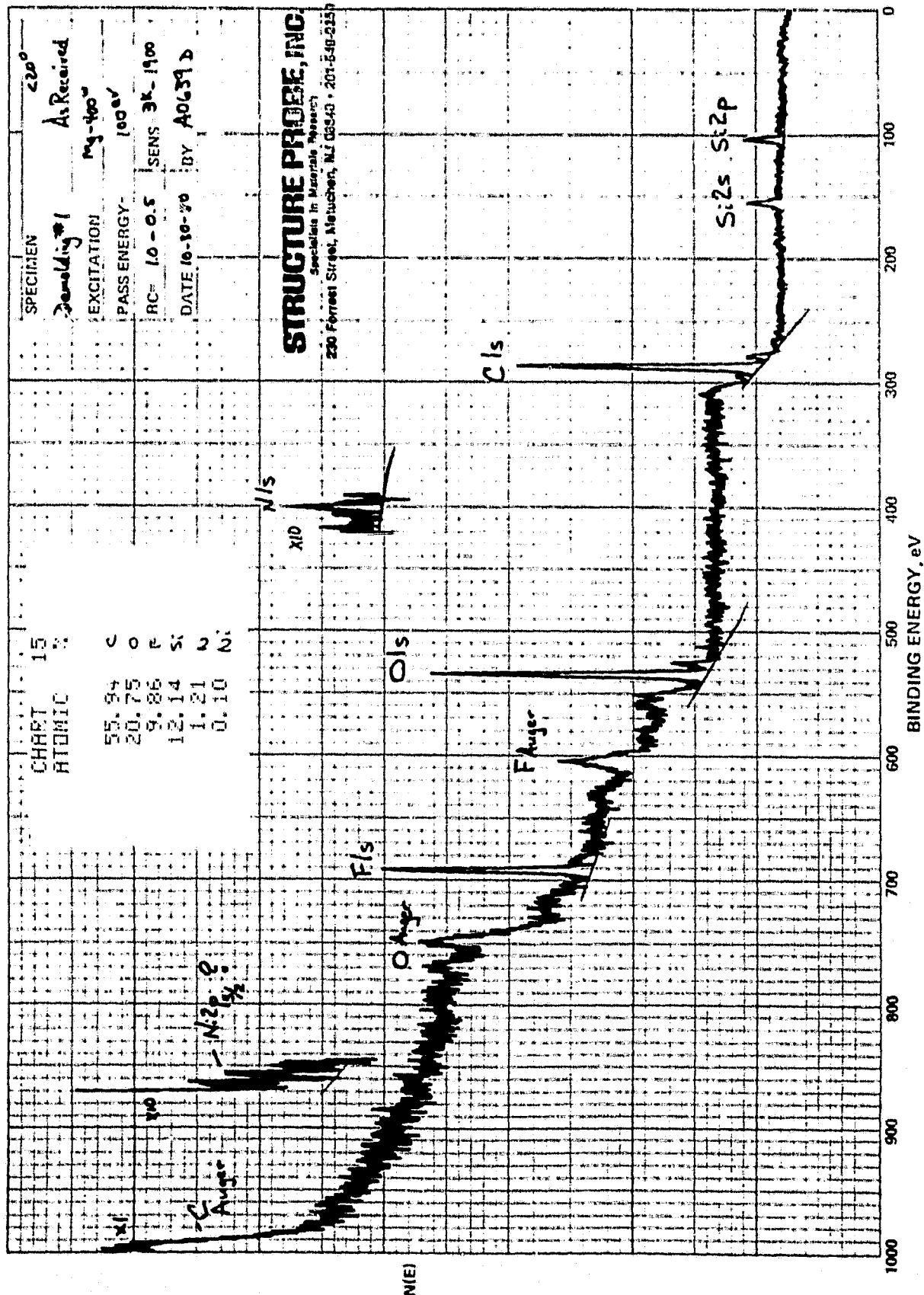
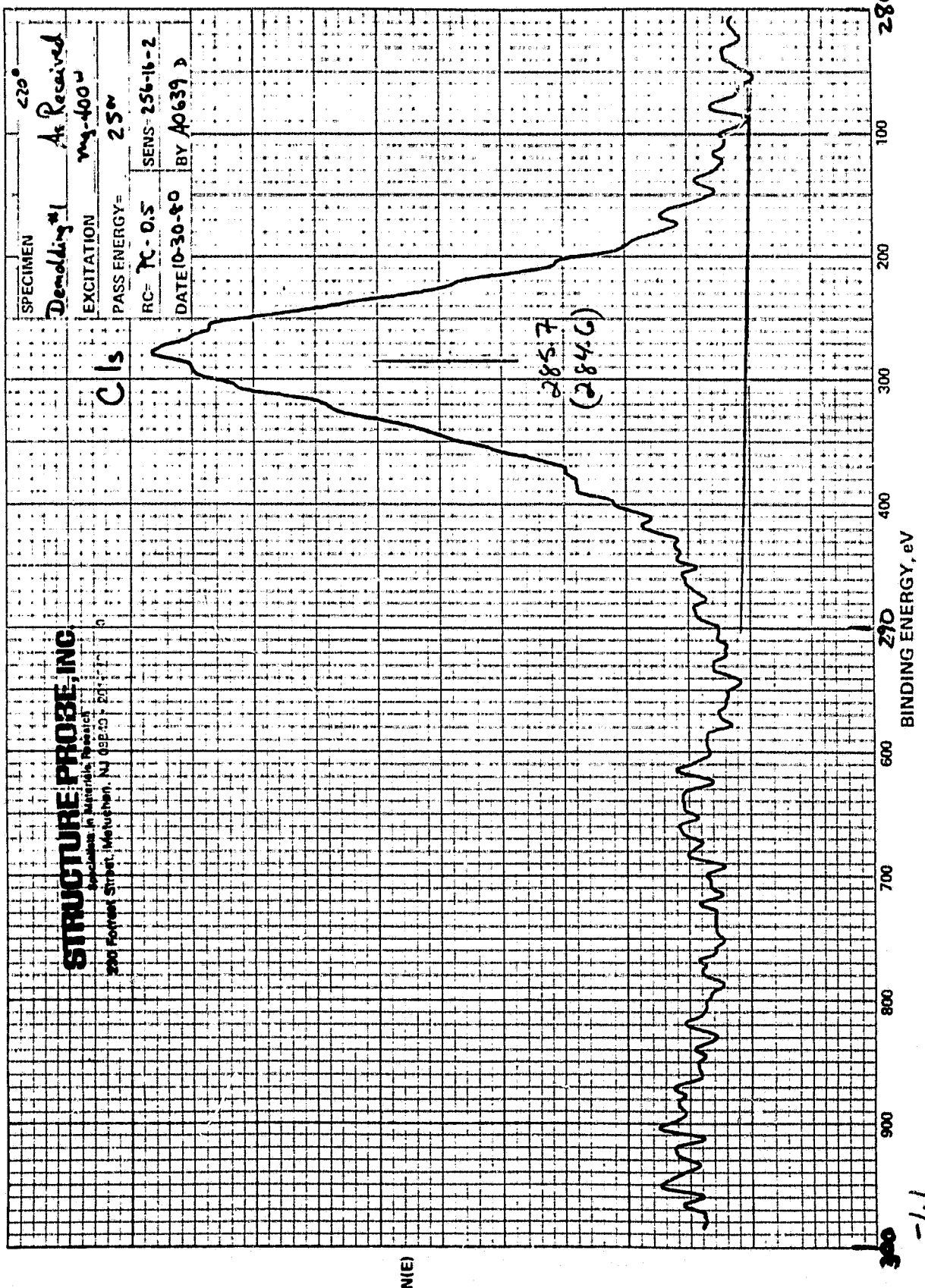


Figure 23

A-6364



PHYSICAL ELECTRONICS INDUSTRIES, INC.
174020



ORIGINAL PAGE IS
OF POOR QUALITY

Figure 24

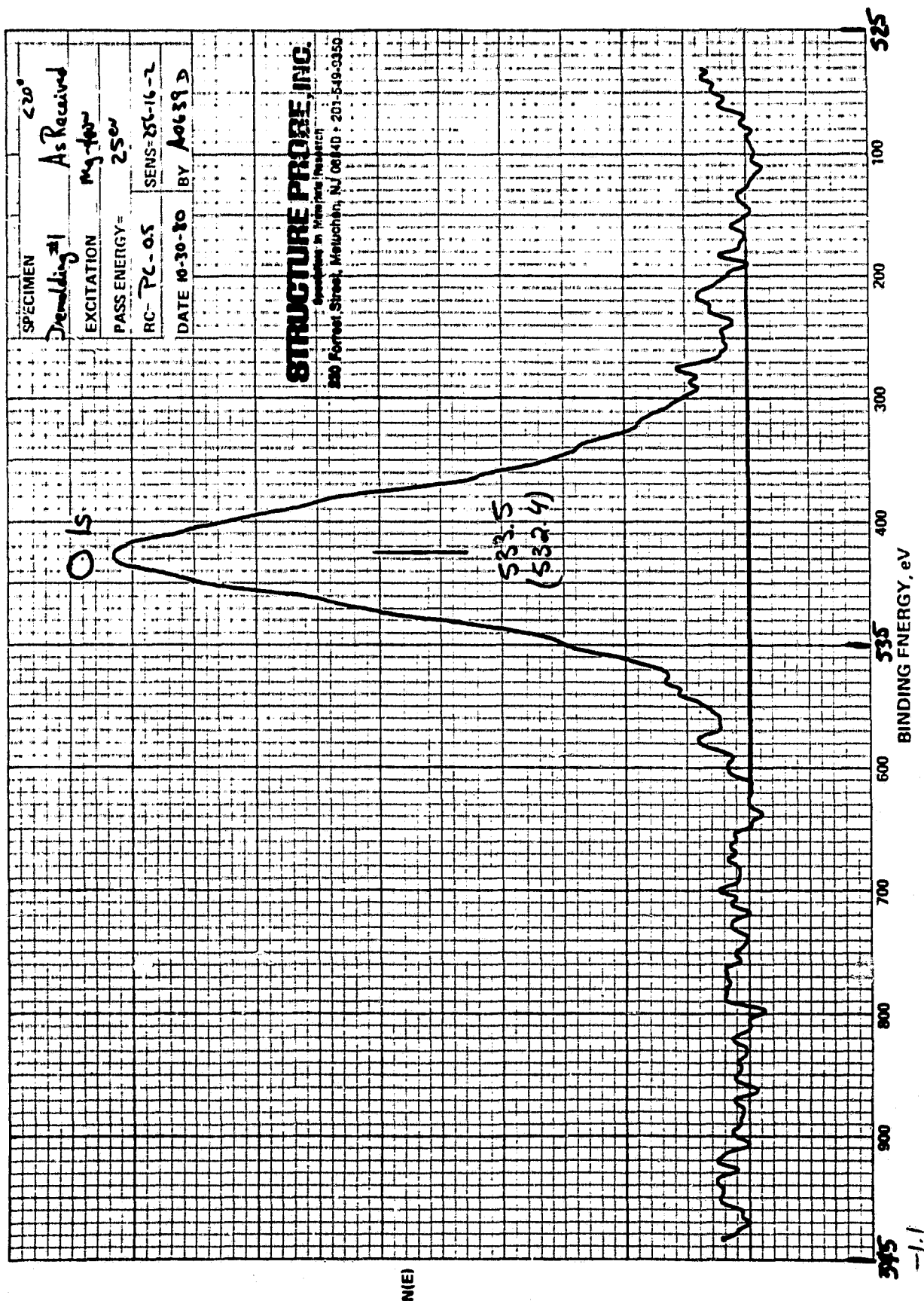
ORIGINAL PAGE IS
OF POOR QUALITY


Figure 25

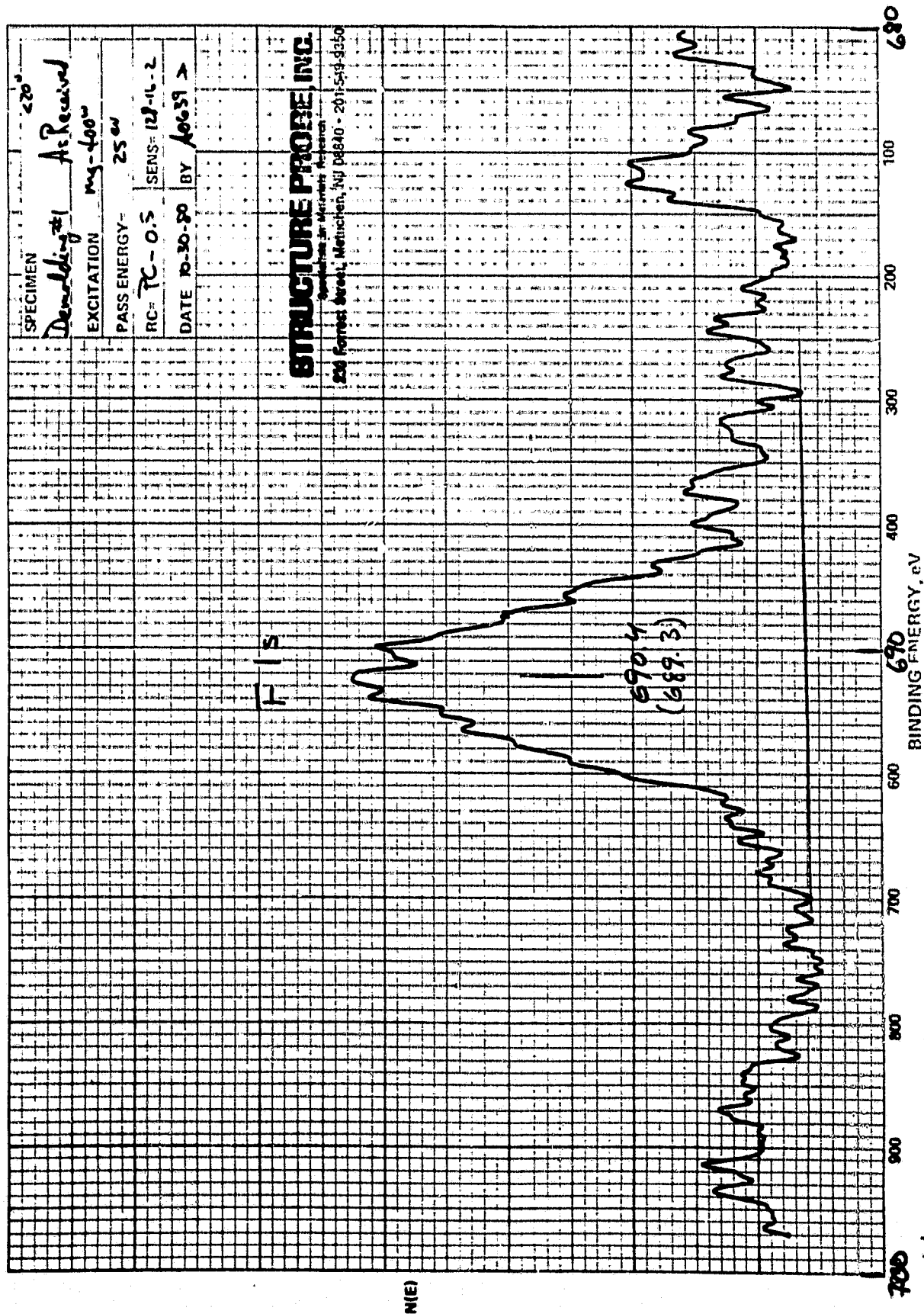
ORIGINAL PAGE IS
OF POOR QUALITY


Figure 26

ORIGINAL PAGE IS
OF POOR QUALITY

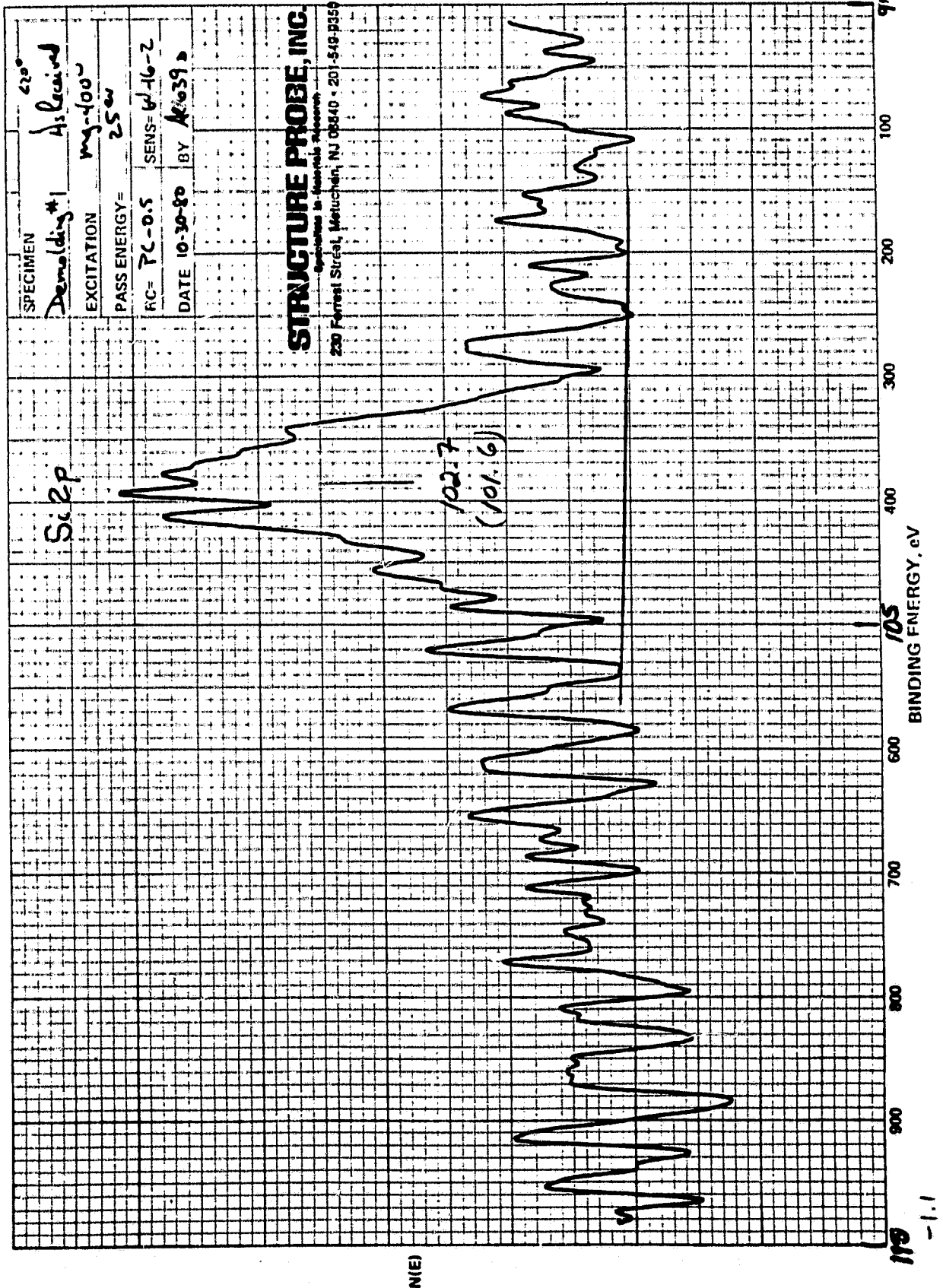


Figure 27

A-6368

ORIGINAL PAGE IS
OF PCOR QUALITY

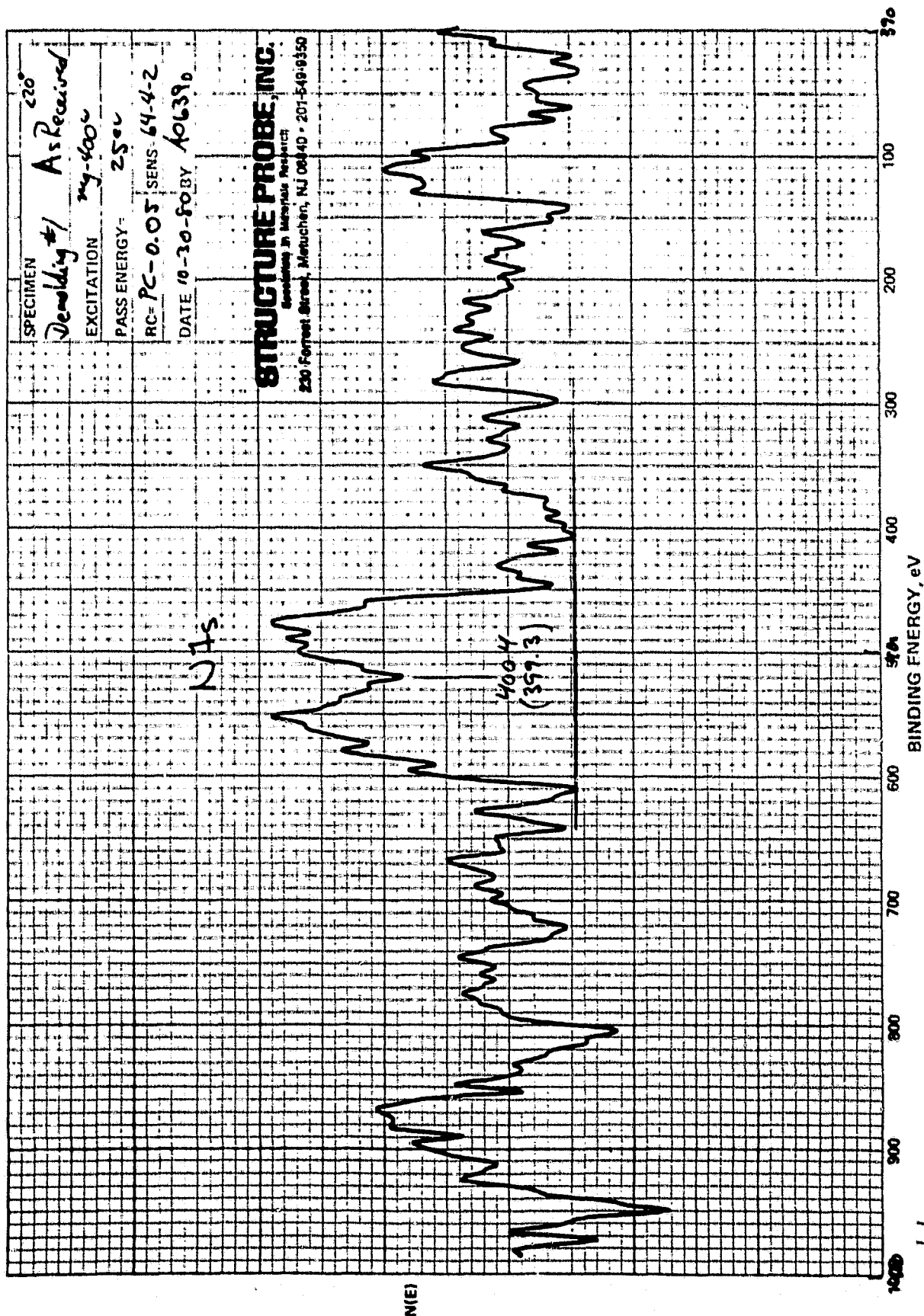


Figure 28

STRUCTURE PROBE, INC.
Specialists in Vacuum Research
200 Forest Street, Metuchen, N.J. 08840

SPECIMEN Remolding 2 As Received
EXCITATION Mg-400W
PASS ENERGY 100 eV
RC 7.0 - 0.5 **SENS** 3E-19A
DATE 10-30-80 **BY** J0639E

CHAFT ATOMIC

Element	Binding Energy (eV)	Intensity	Area	Conc.
C 1s	64.94	20.48	14.24	0.32
O 1s	53.32	20.48	14.24	0.32
Si 2p	103.0	20.48	14.24	0.32

Figure 29

A-6370

PHYSICAL ELECTRONICS INDUSTRIES, INC.
174020

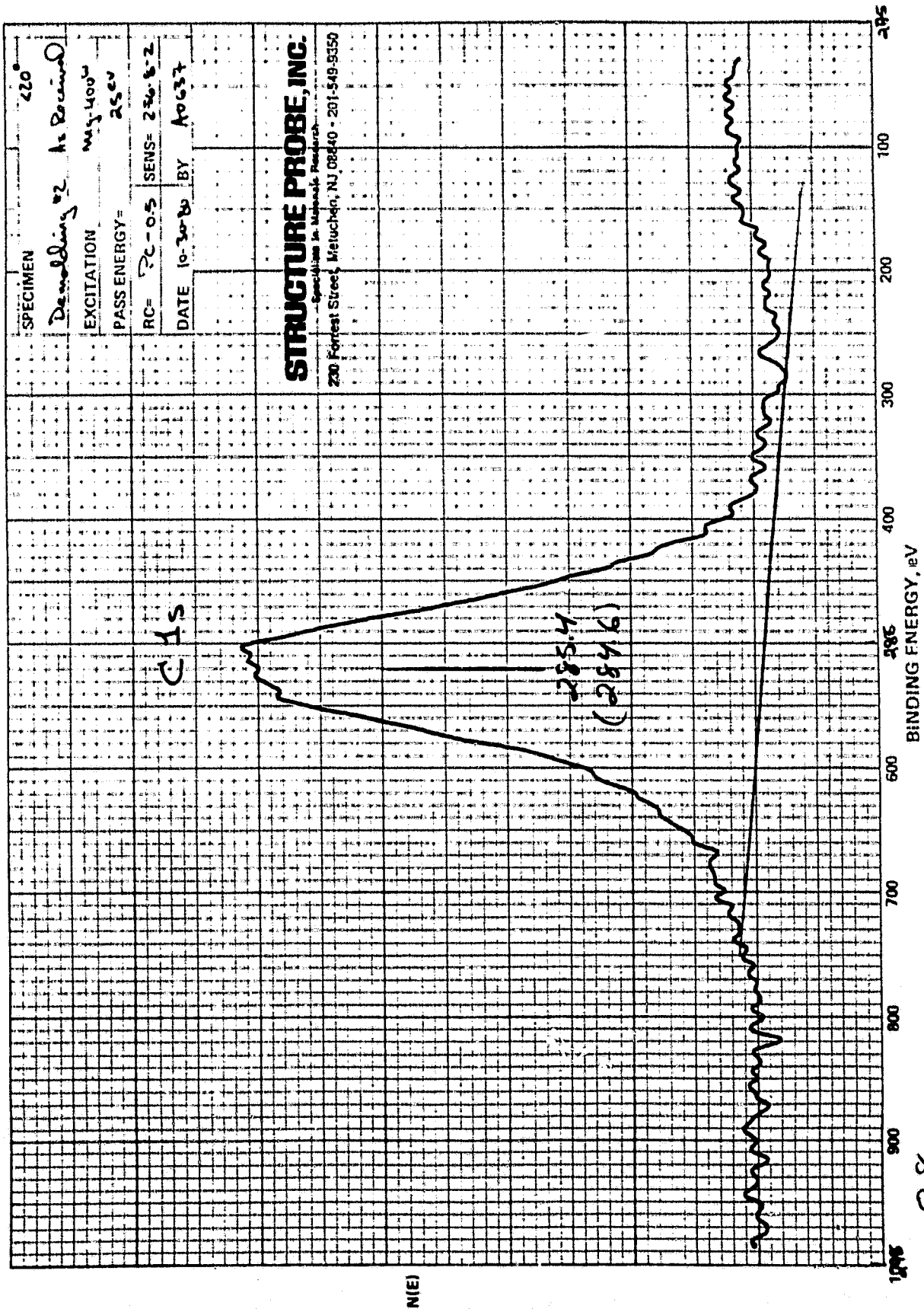


Figure 30

ORIGINAL PAGE IS
OF POOR QUALITY

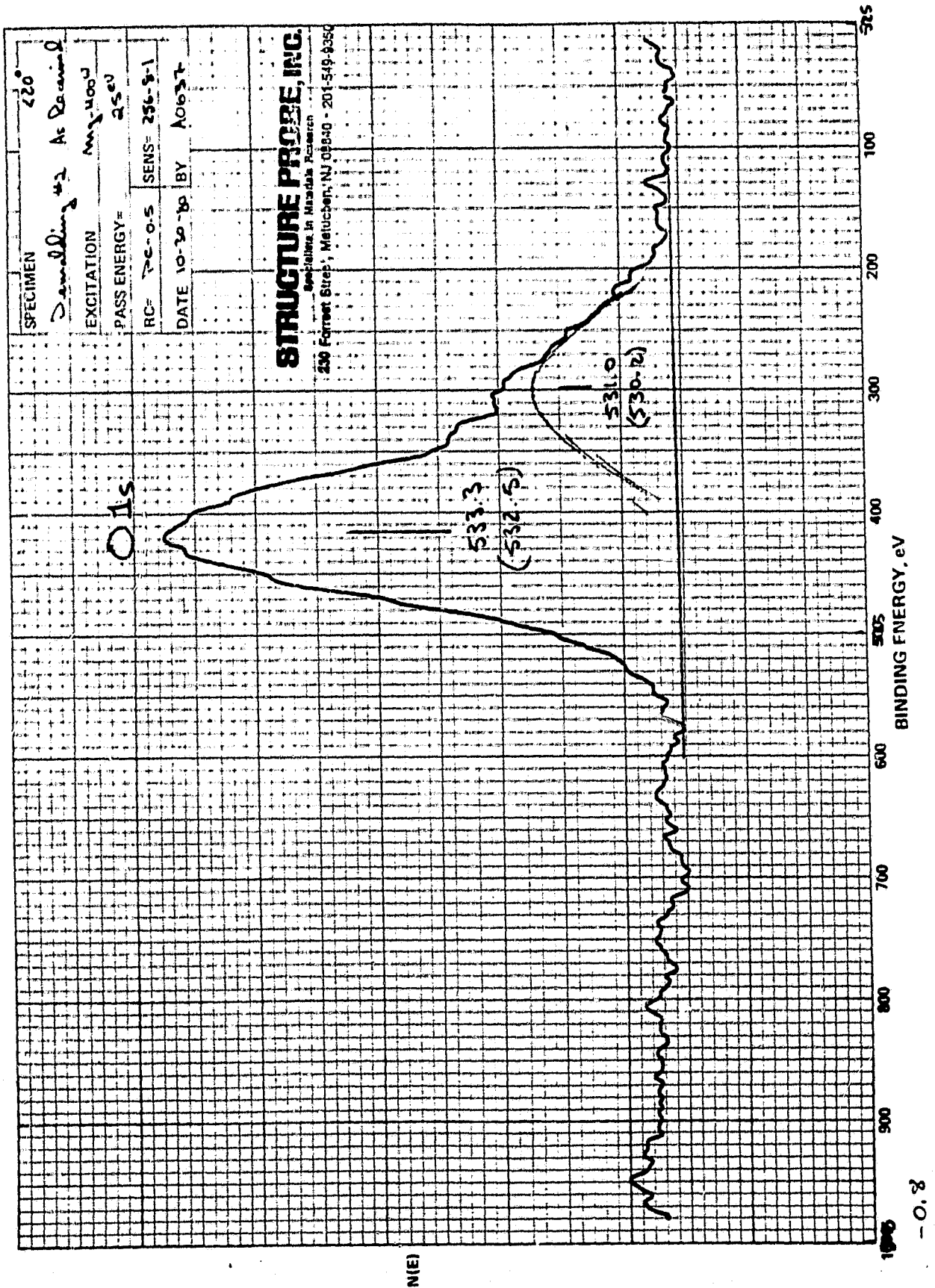


Figure 31

ORIGINAL IS
OF POOR QUALITY

Φ PHYSICAL ELECTRONICS INDUSTRIES, INC.
174020

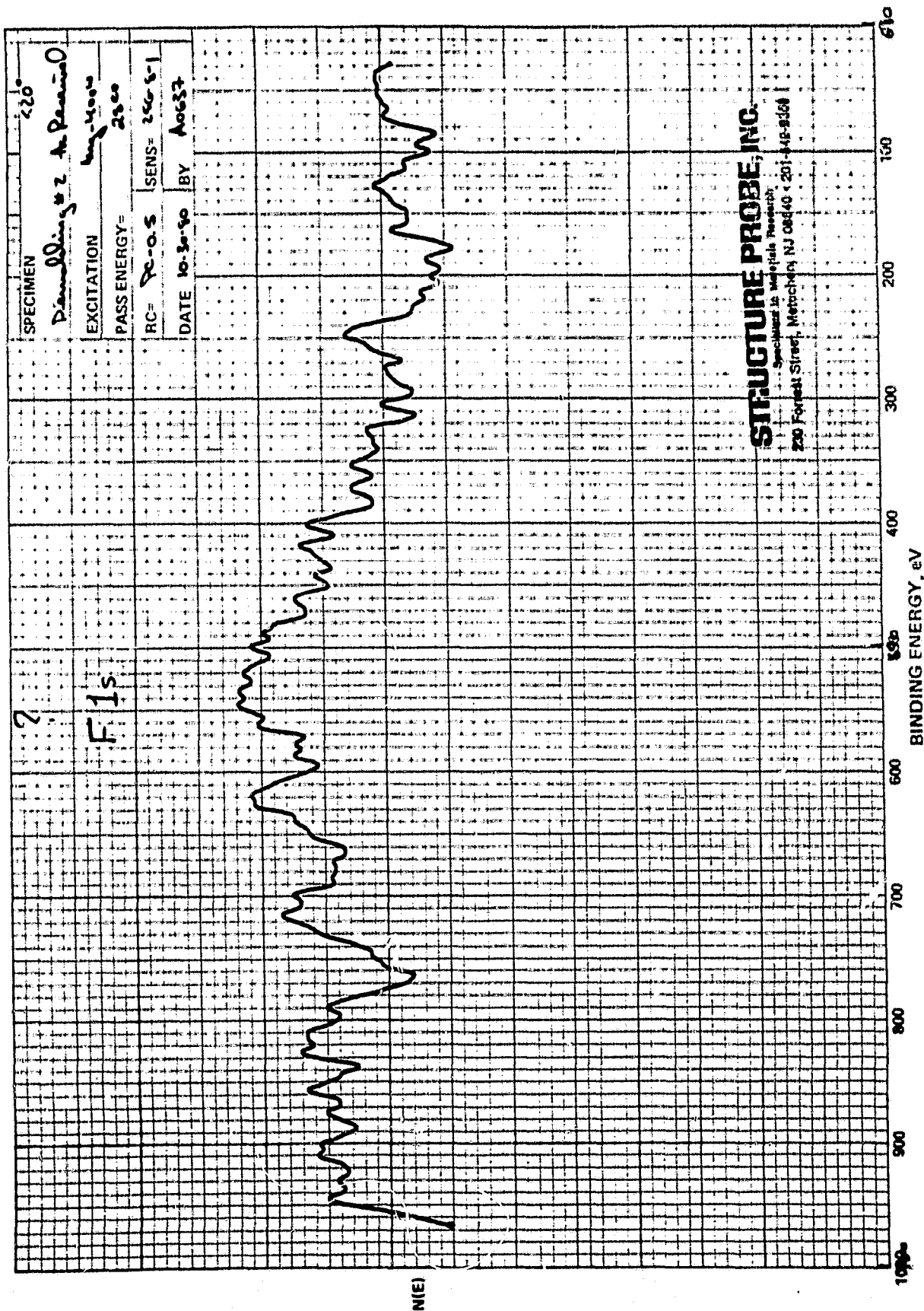


Figure 32

A-6373

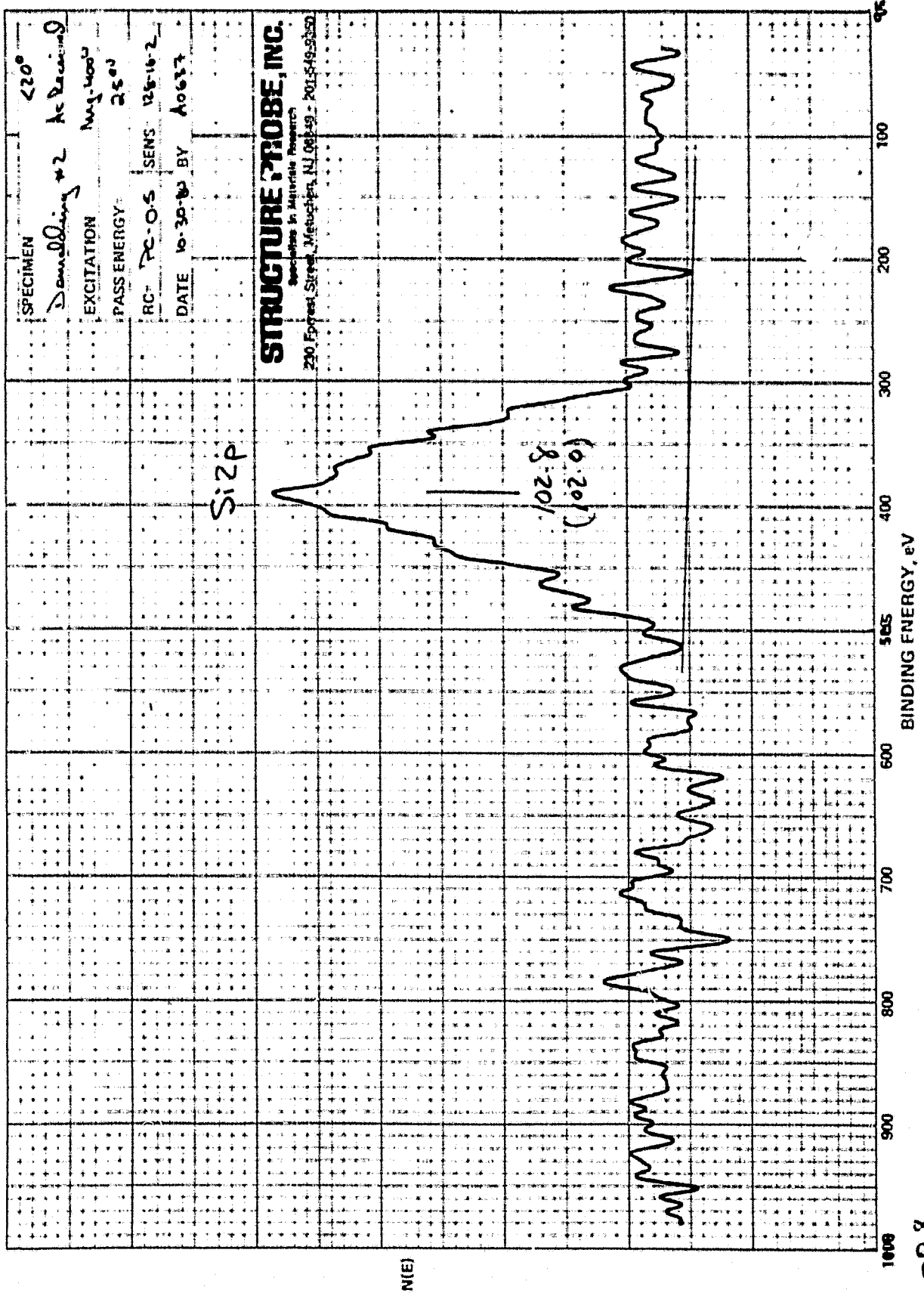


Figure 33



PHYSICAL ELECTRONICS INDUSTRIES, INC.
174020

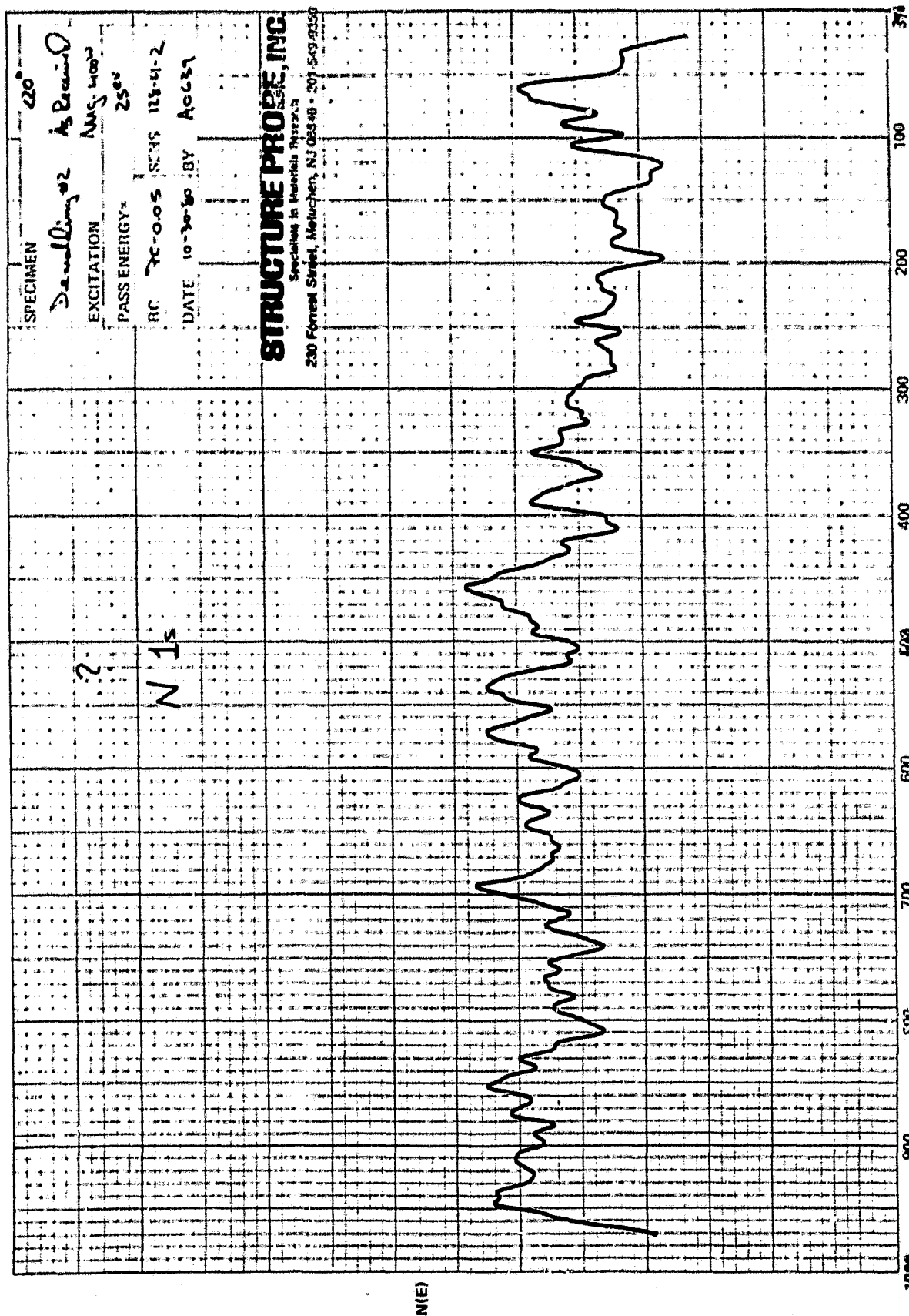


Figure 34

ORIGINAL PAGE IS
OF POOR QUALITY

A-6375

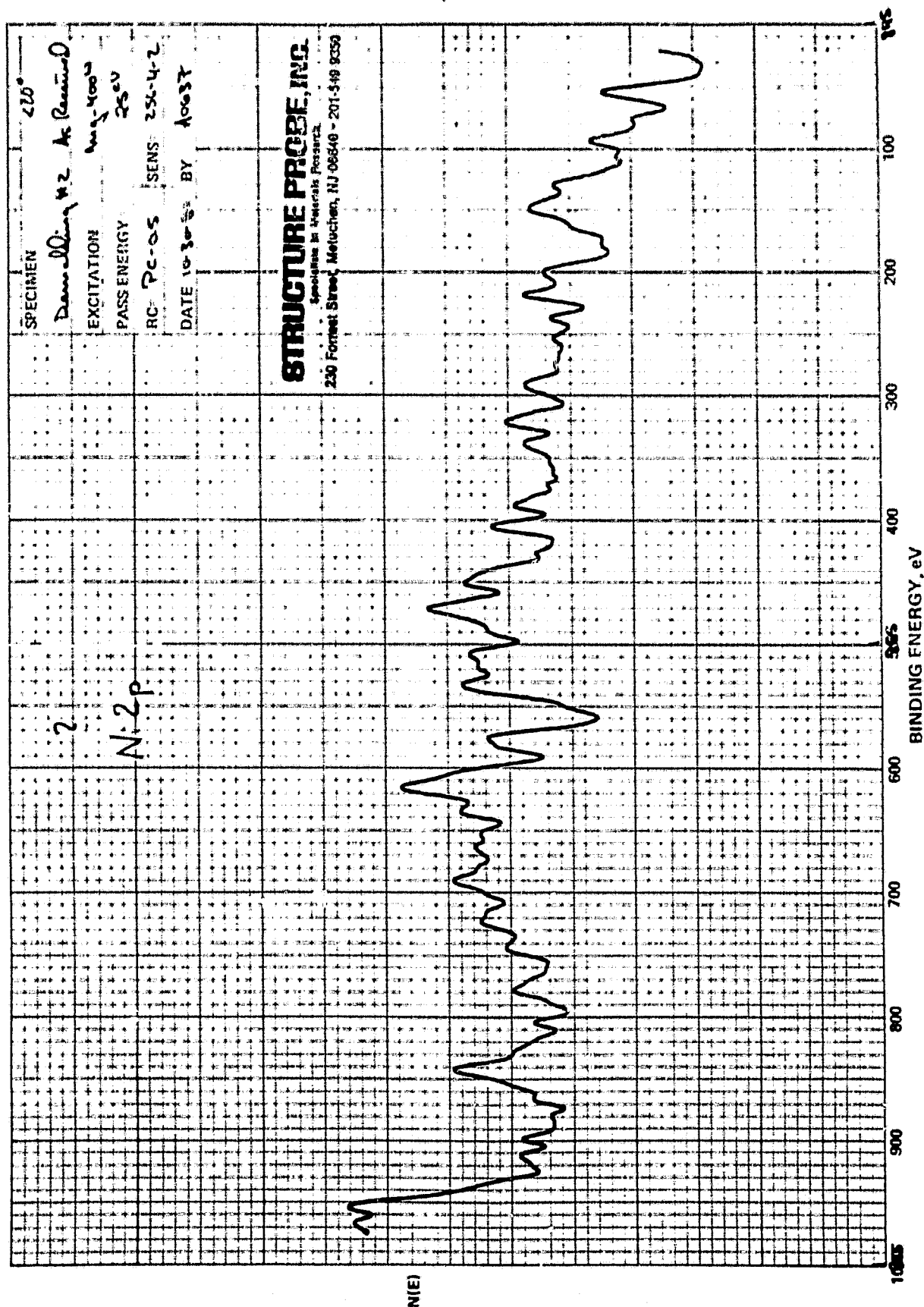


Figure 35

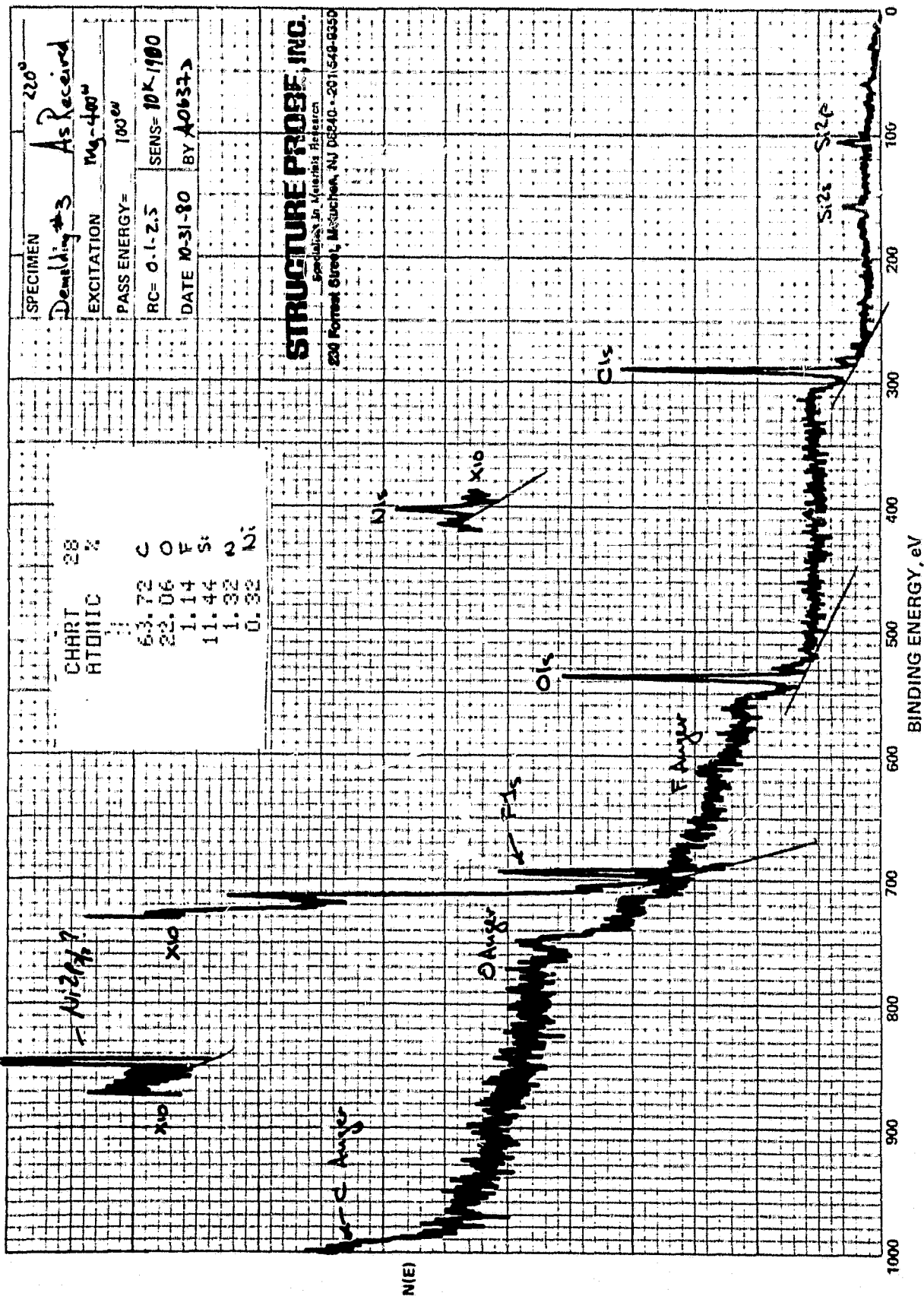
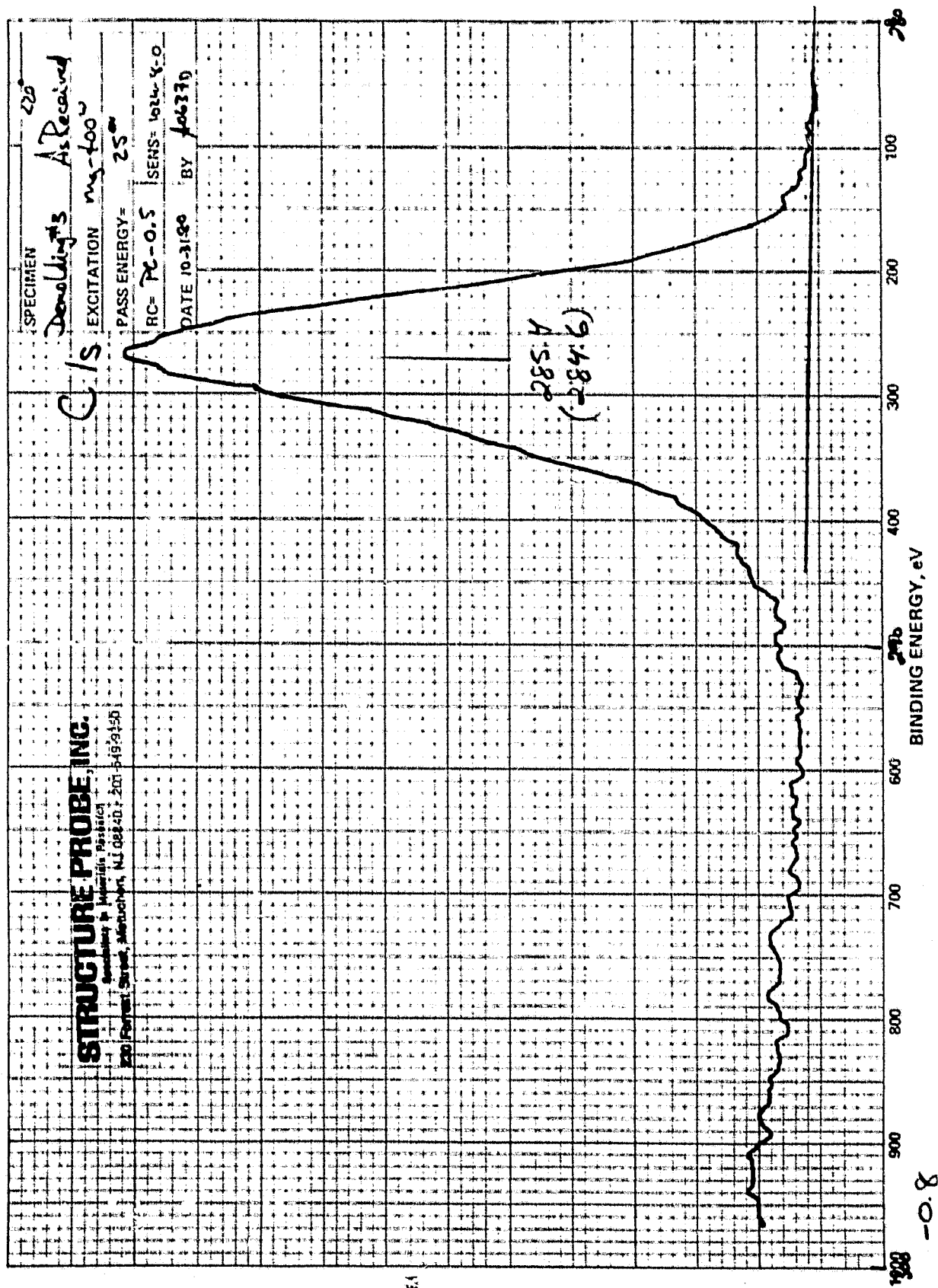


Figure 35



ORIGINAL PAGE IS
OF POOR QUALITY

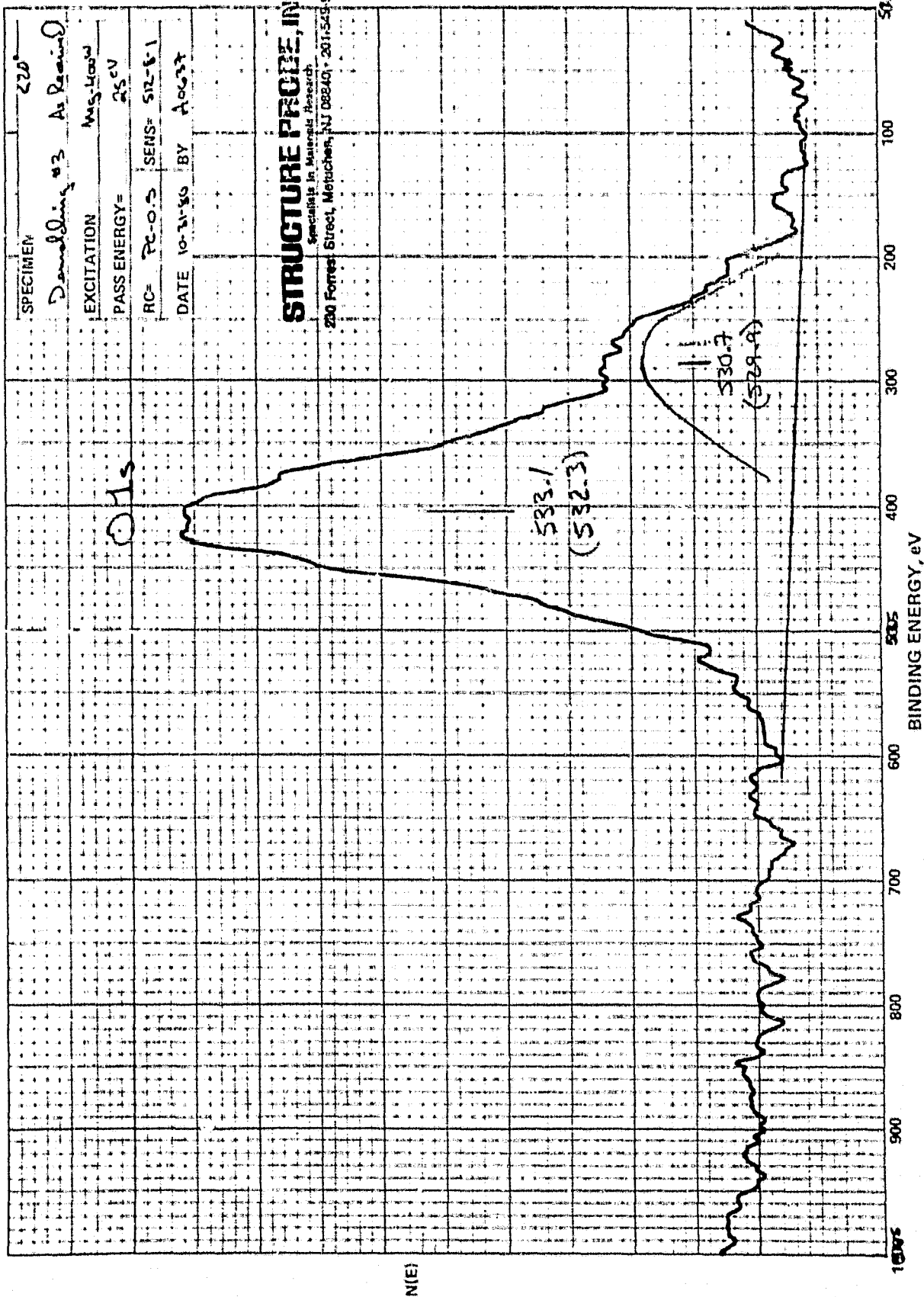


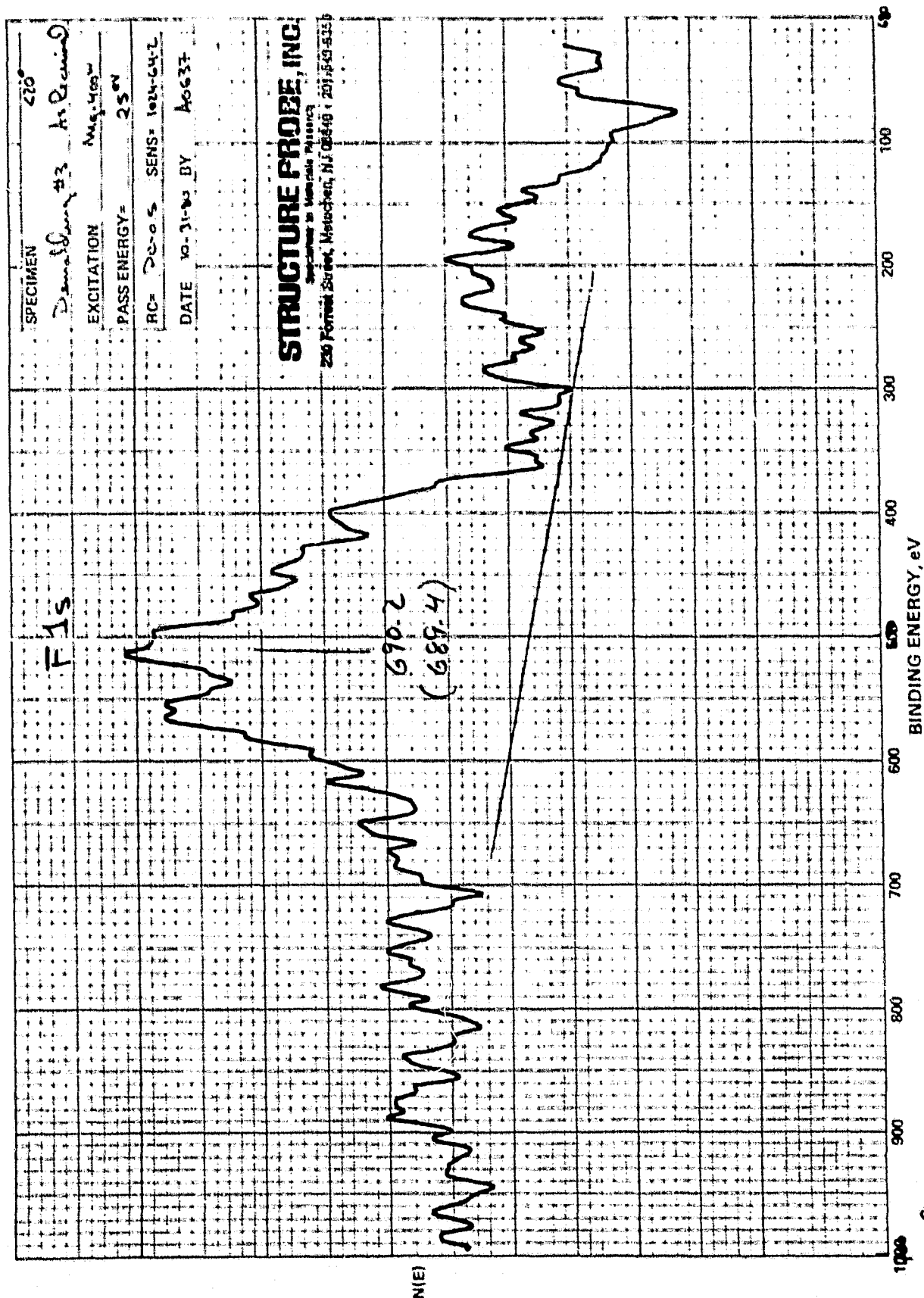
Figure 38



PHYSICAL ELECTRONICS INDUSTRIES, INC.
174020

A-6379

ORIGINAL PAGE IS
OF POOR QUALITY



ORIGINAL PAGE IS
OF POOR QUALITY

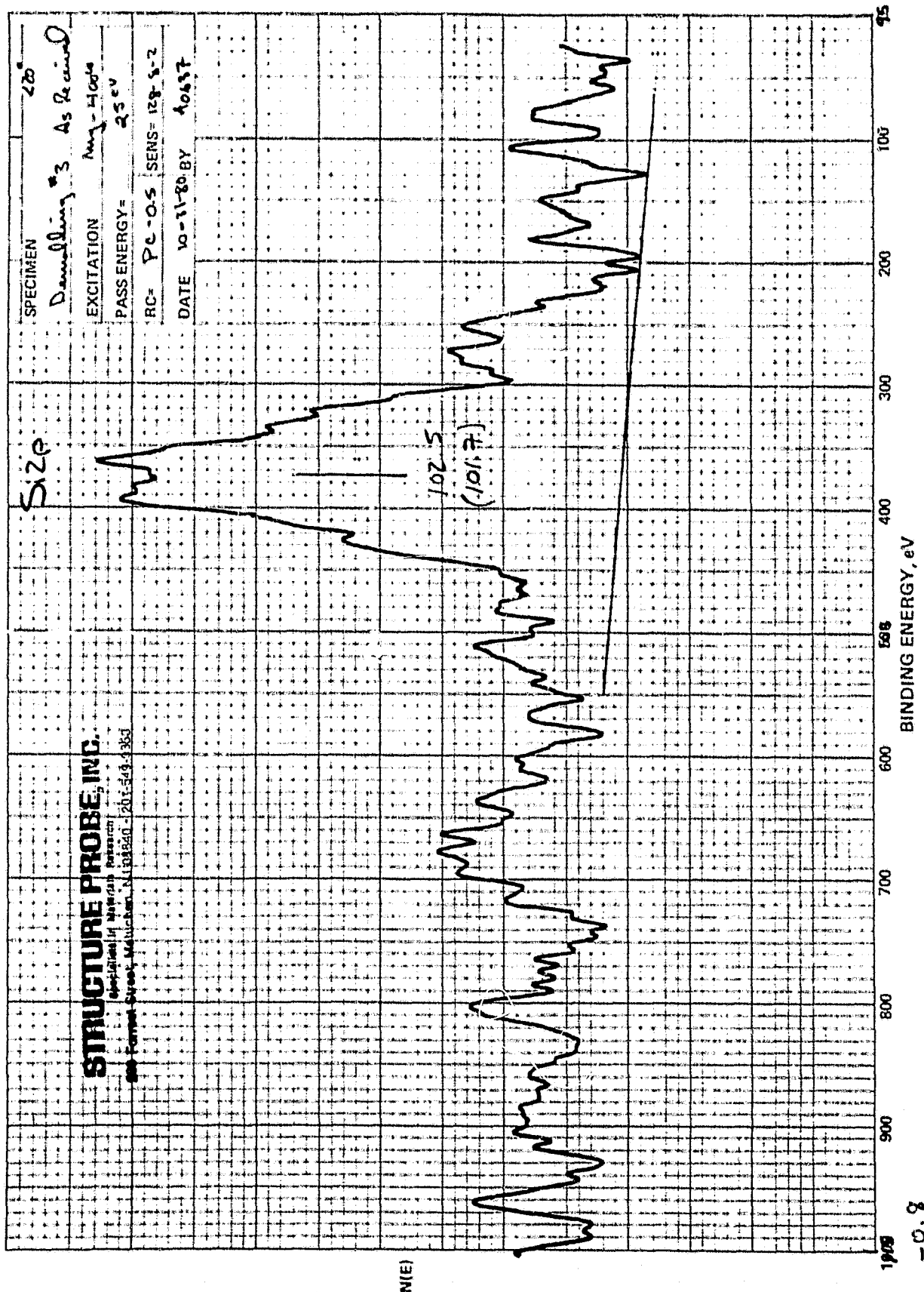


Figure 40

A-6381

PHYSICAL ELECTRONICS INDUSTRIES, INC.
174020

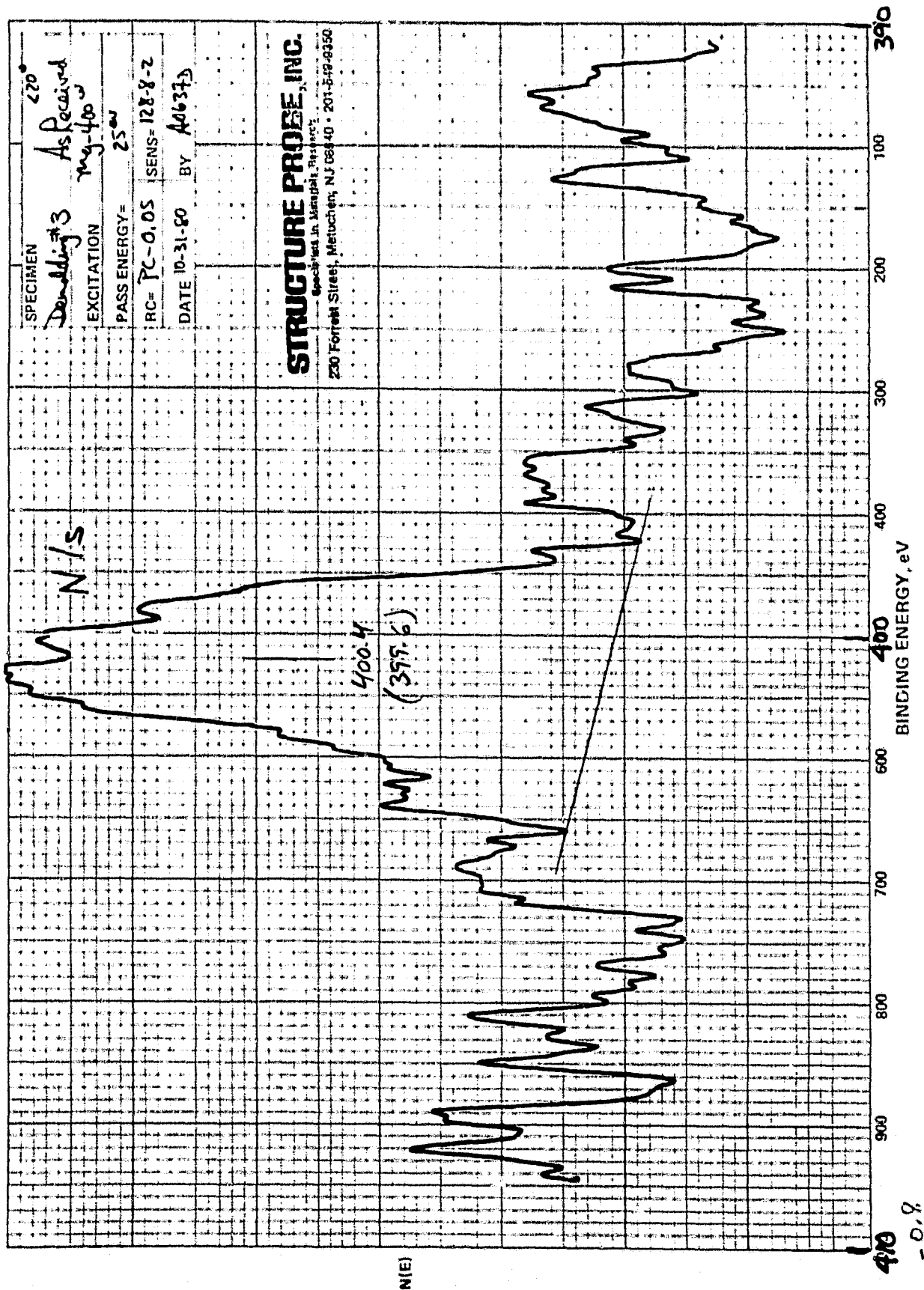


Figure 41

(3)N

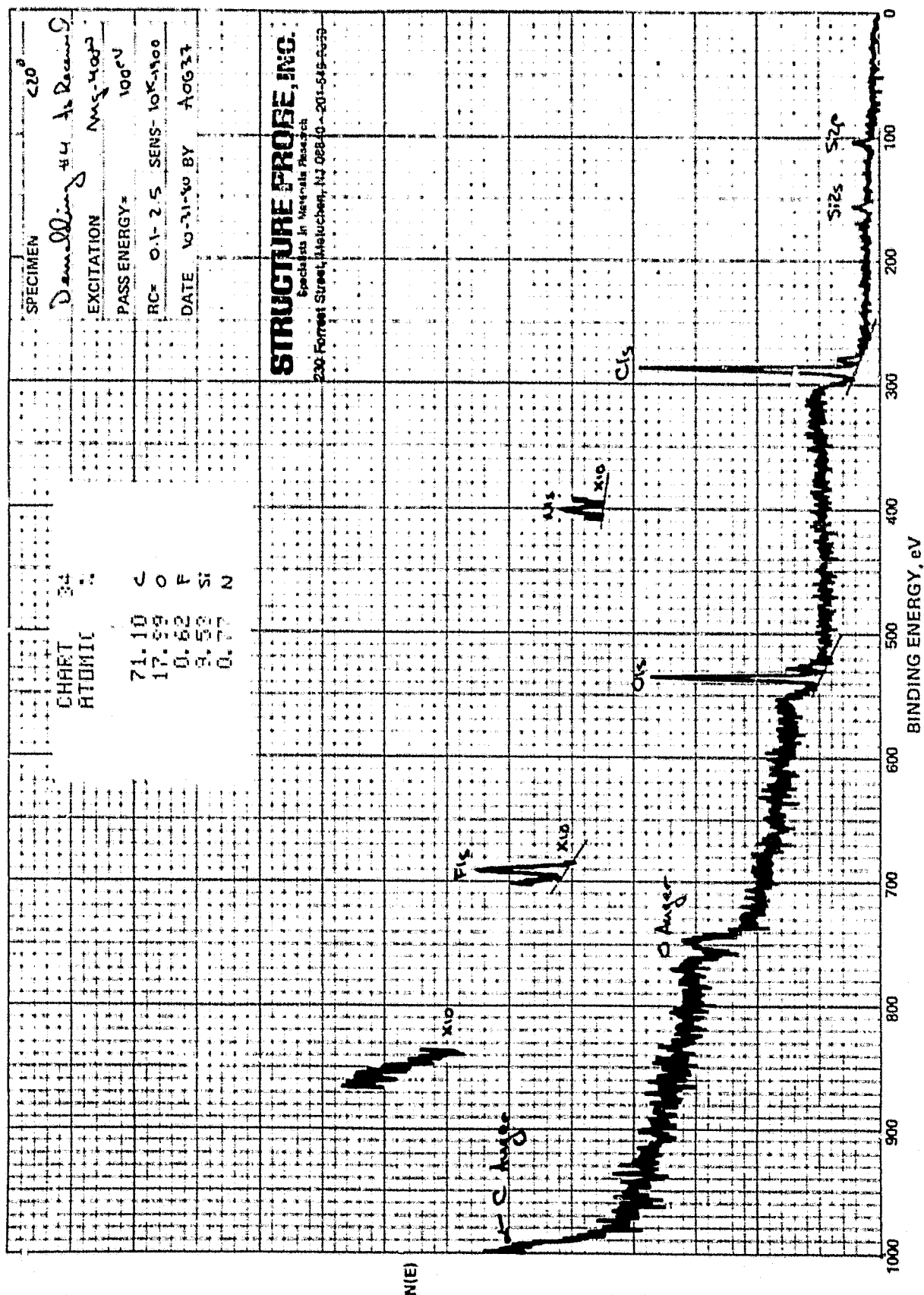


Figure 42

ORIGINAL PAGE IS
OF POOR QUALITY

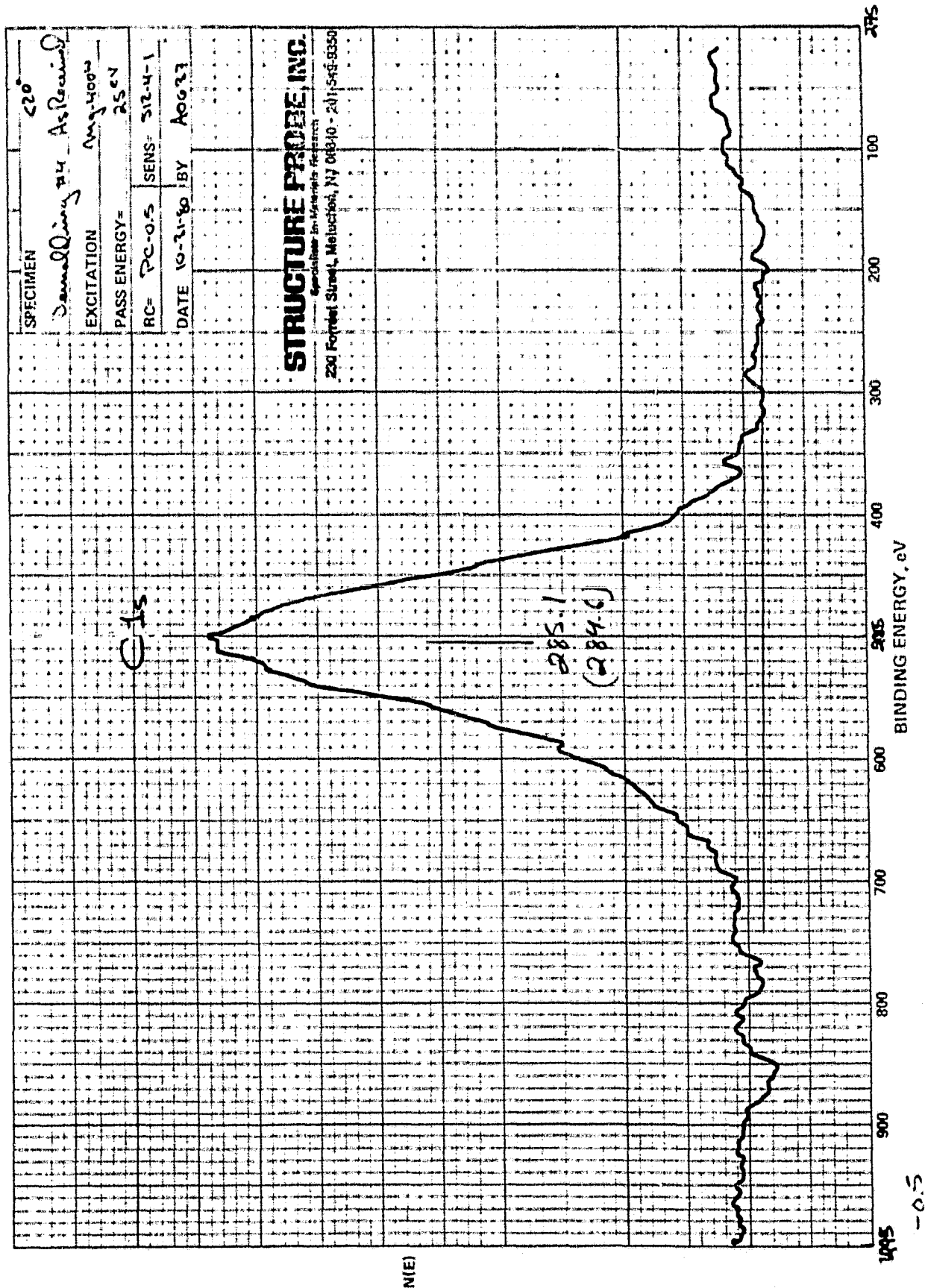


Figure 43

ORIGINAL PAGE IS
OF POOR QUALITY

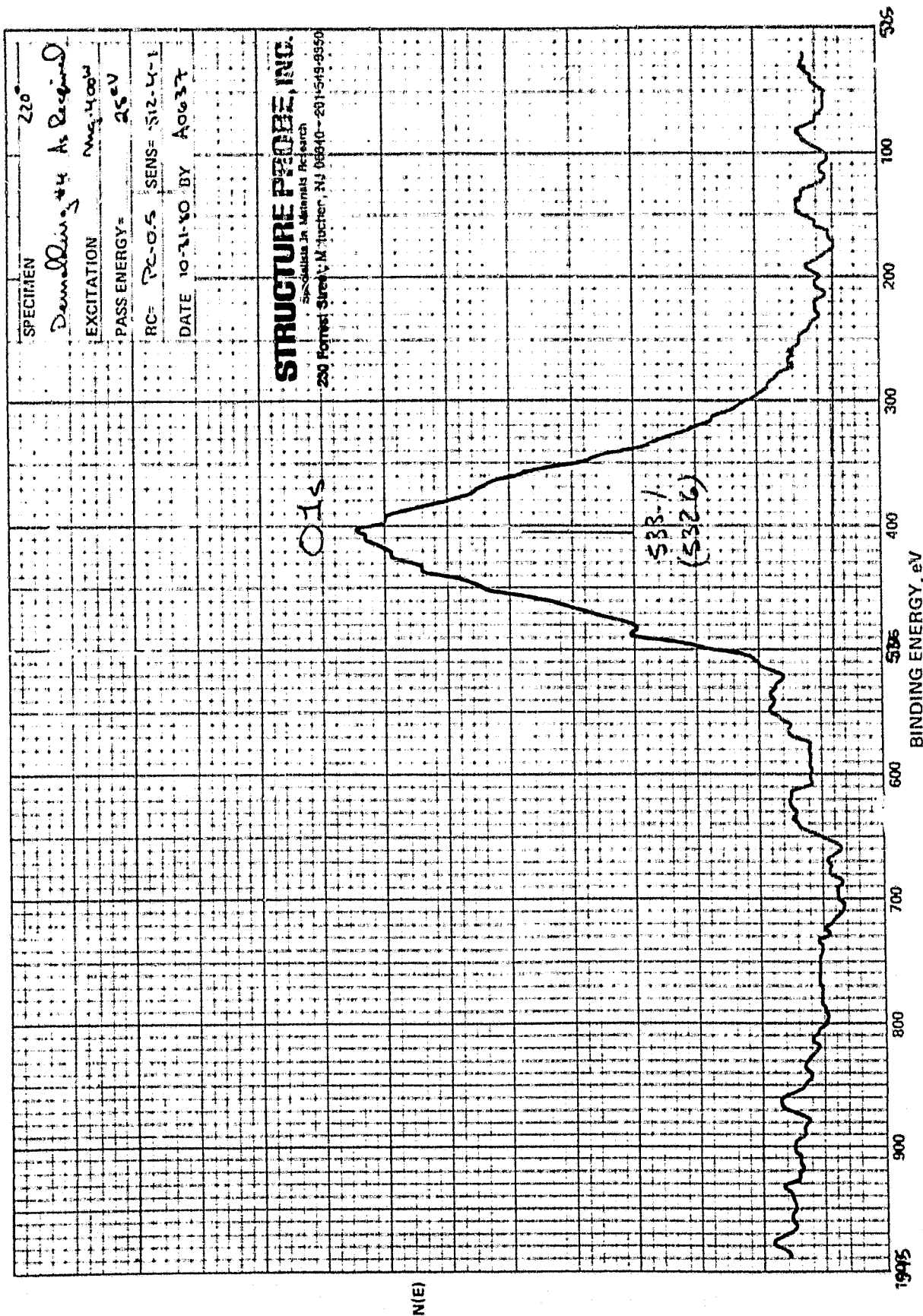


Figure 44

ORIGINAL PAGE IS
OF POOR QUALITY

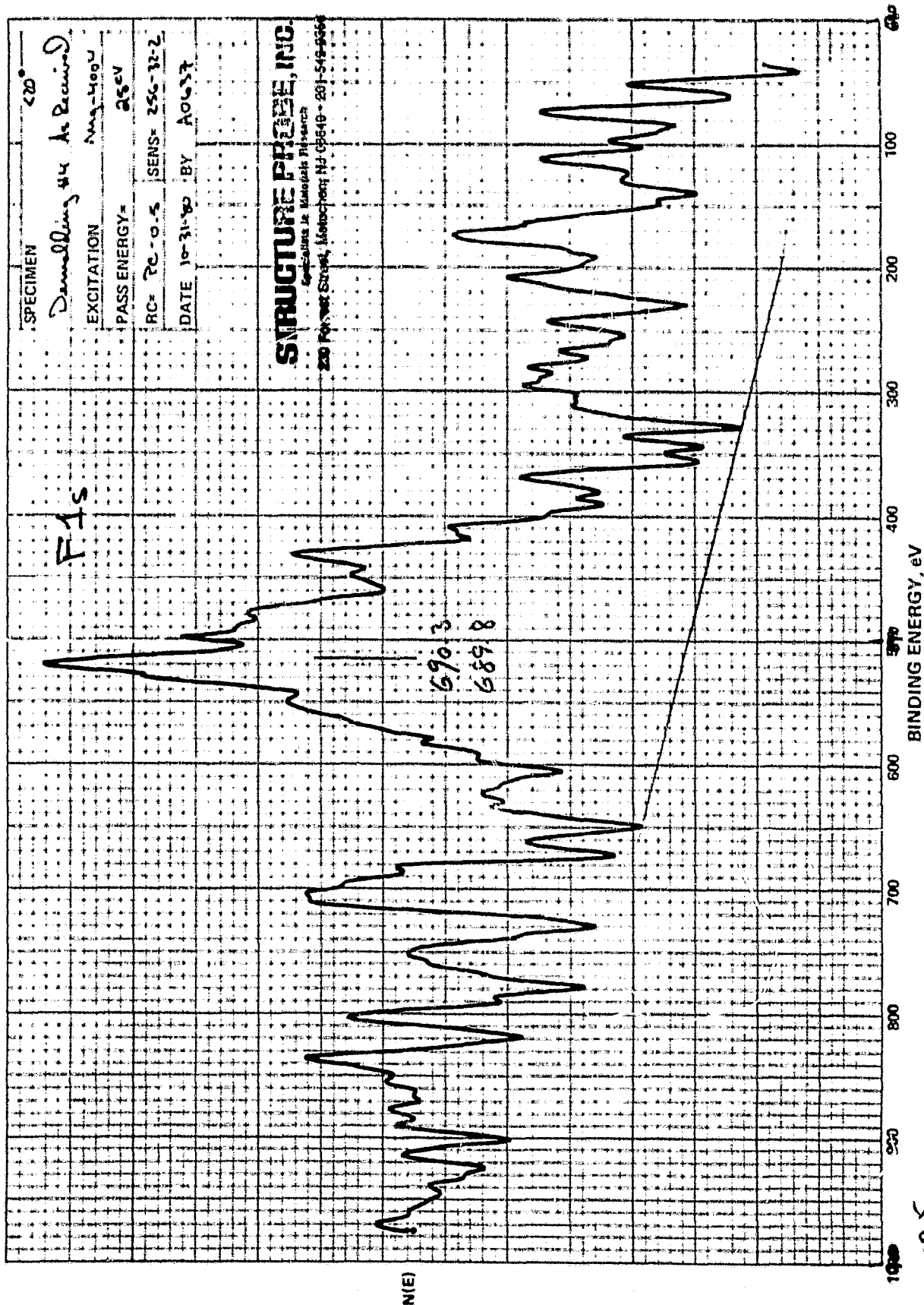


Figure 45

ORIGINAL PAGE IS
OF POOR QUALITY.

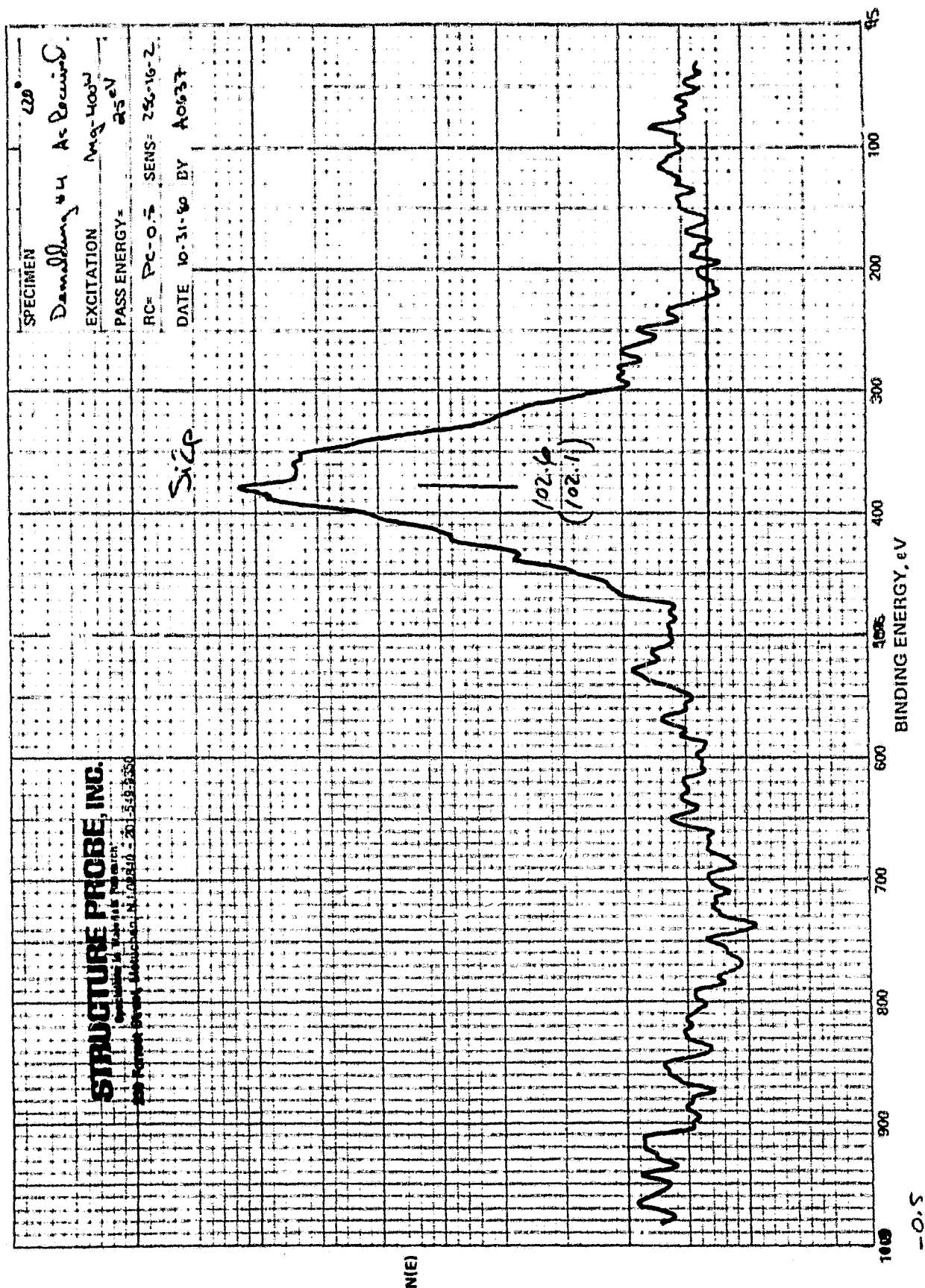


Figure 46

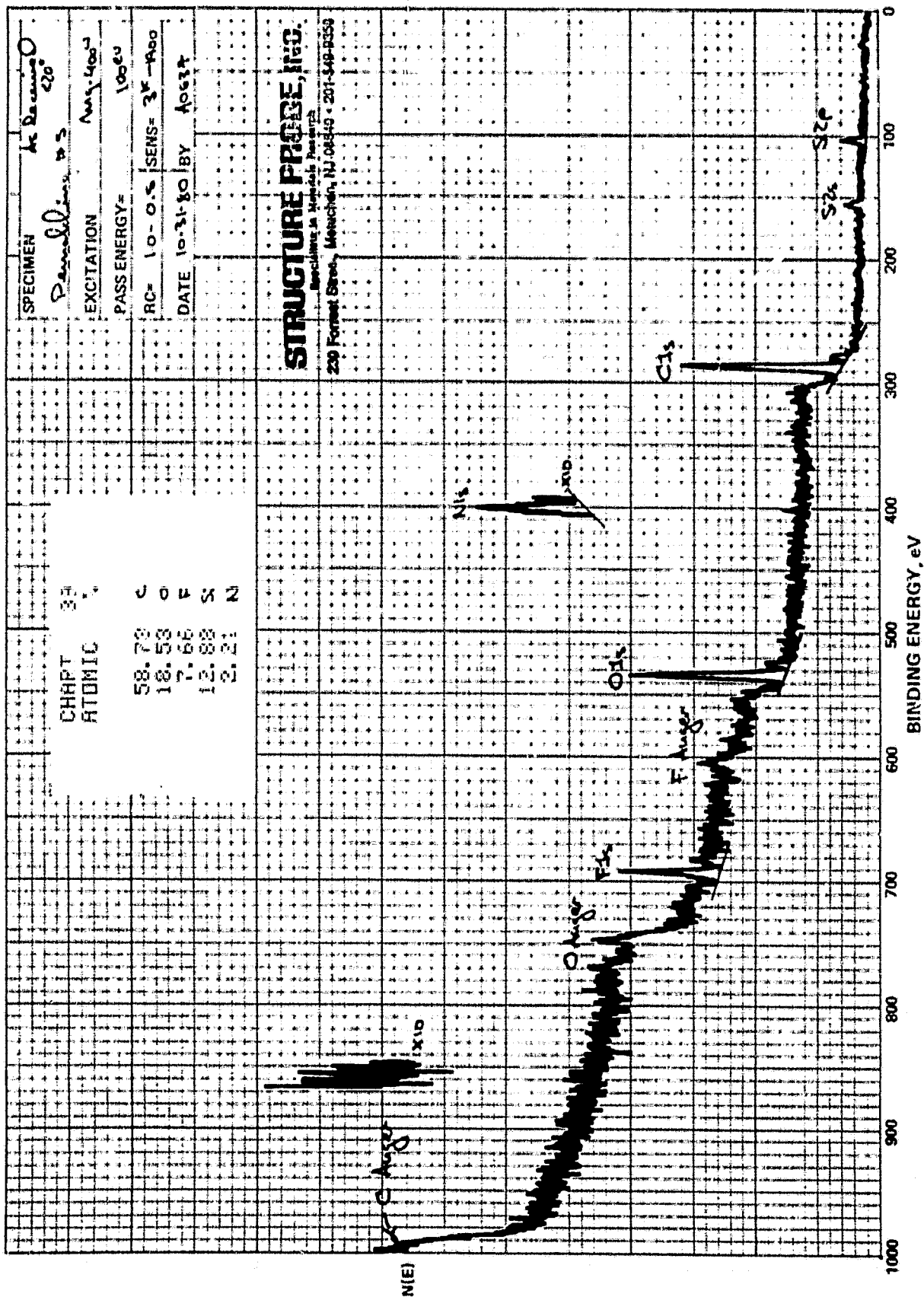
ORIGINAL PAGE IS
OF POOR QUALITY


Figure 47

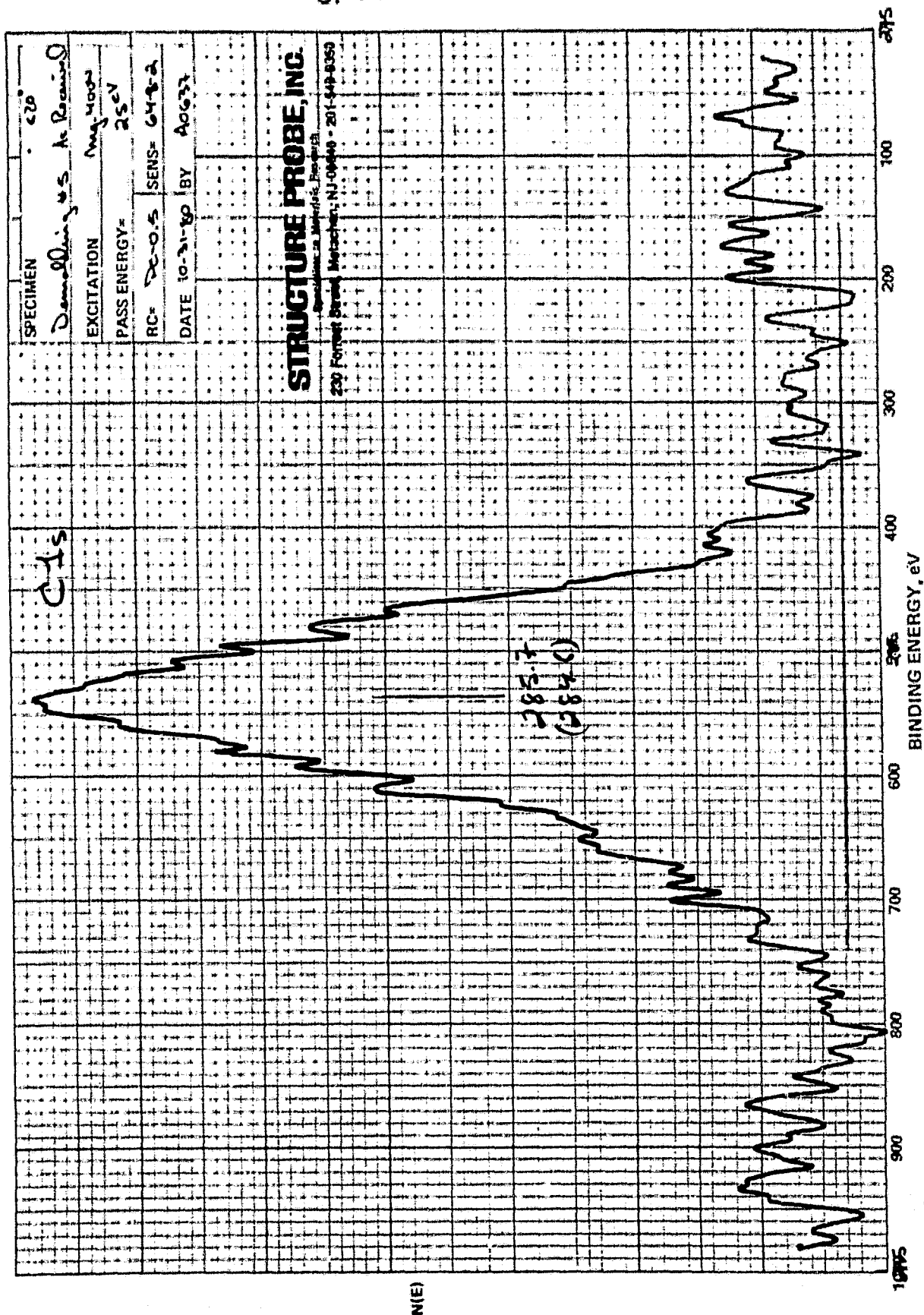
ORIGINAL PAGE IS
OF POOR QUALITY

Figure 48

ORIGINAL PAGE IS
OF POOR QUALITY

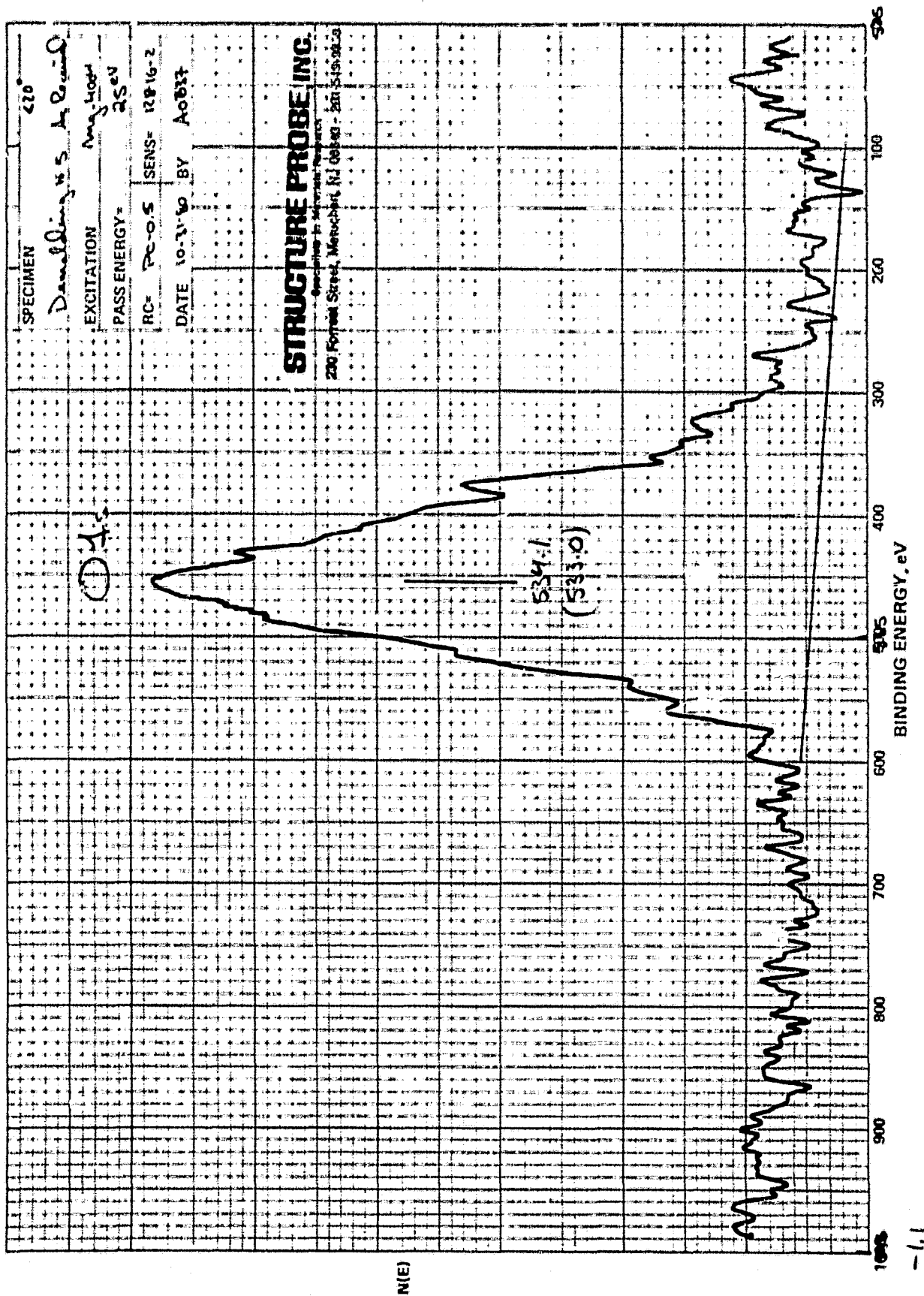


Figure 49

ORIGINAL PAGE IS
OF POOR QUALITY

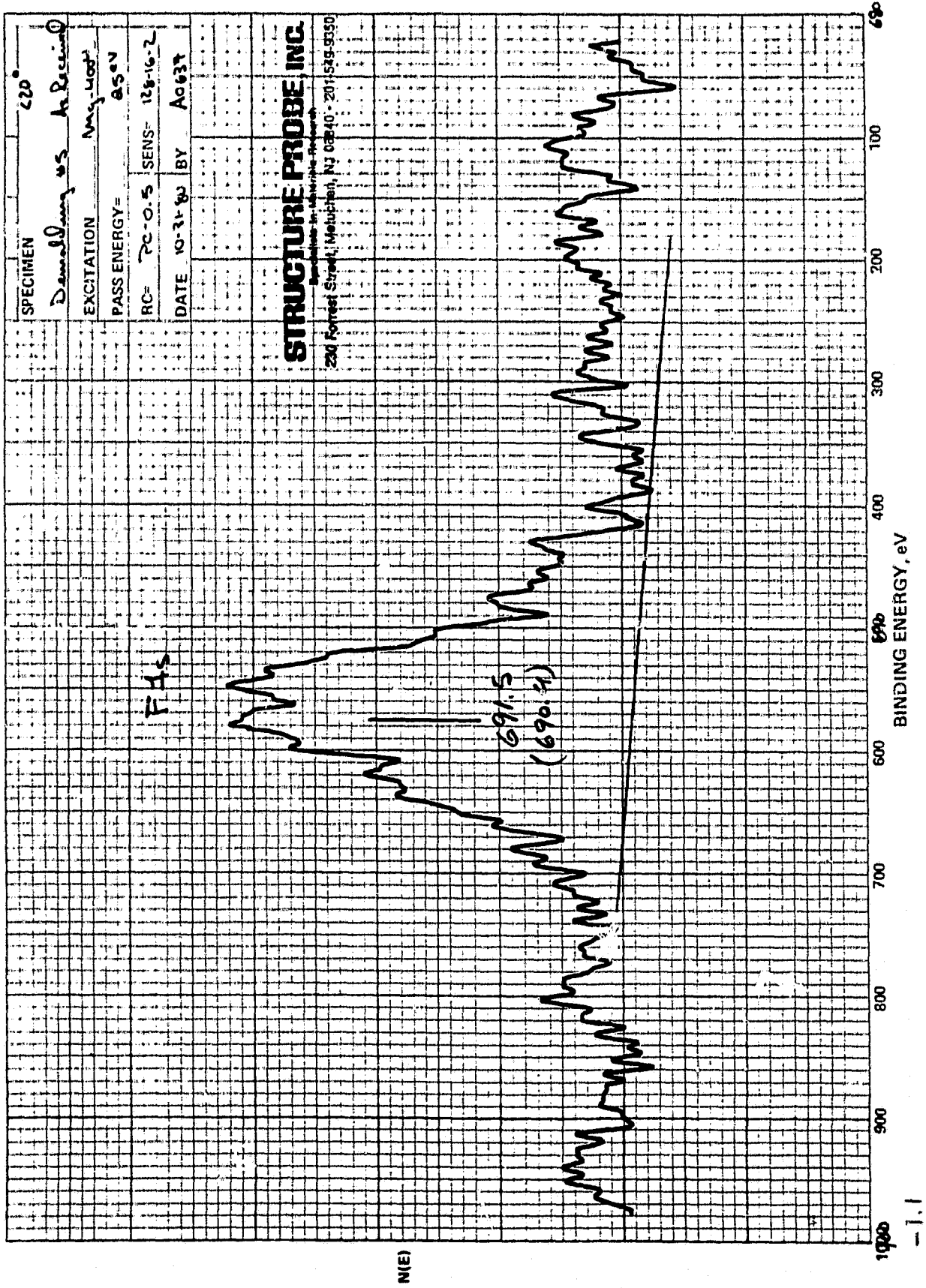


Figure 50

A-6391

Φ PHYSICAL ELECTRONICS INDUSTRIES, INC.
174020

STRUCTURE PROBE, INC.

200 Forest Street, Menlo Park, NJ 08040 • 201-549-9350
Specialists in Materials Research

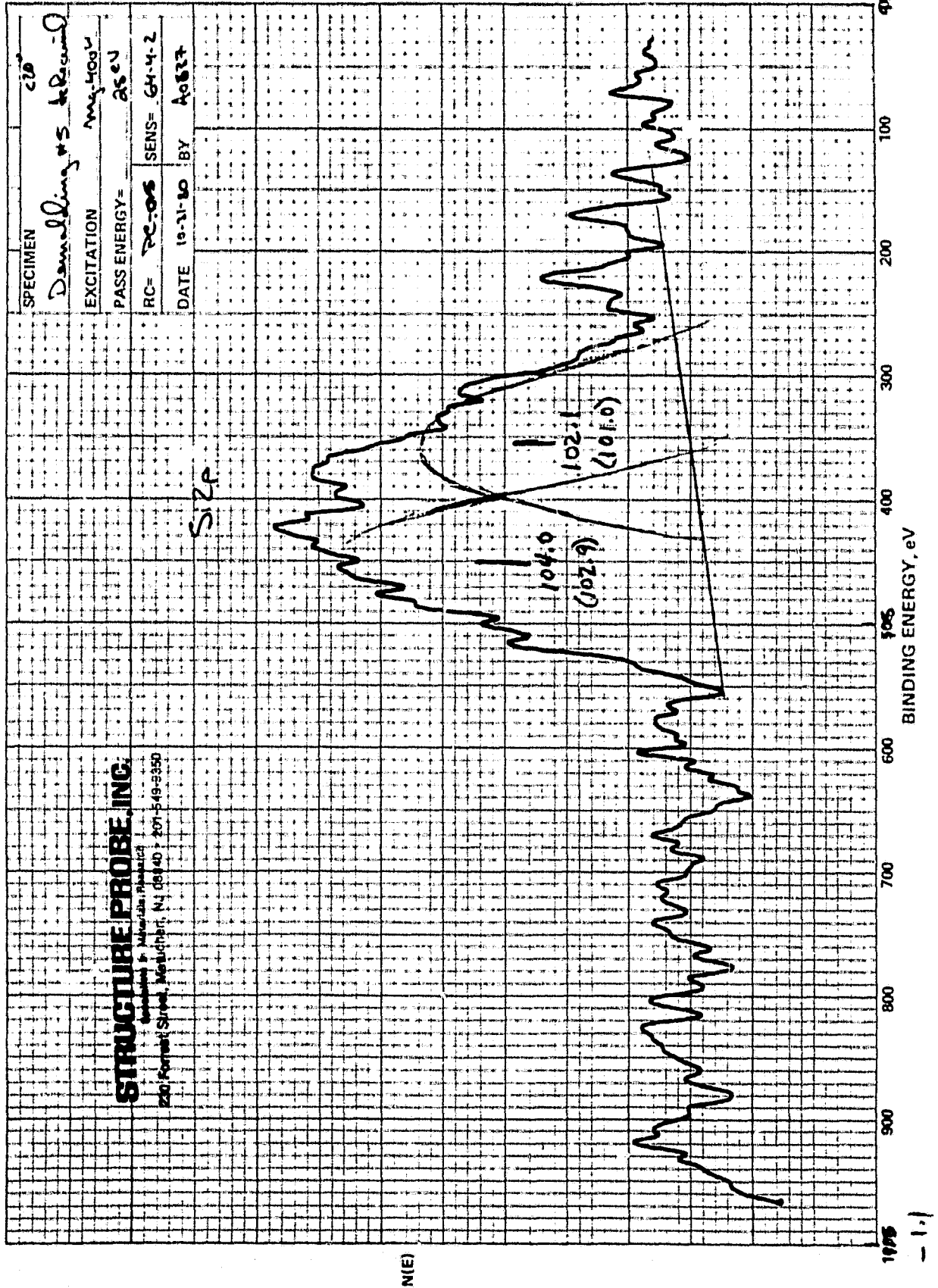


Figure 51

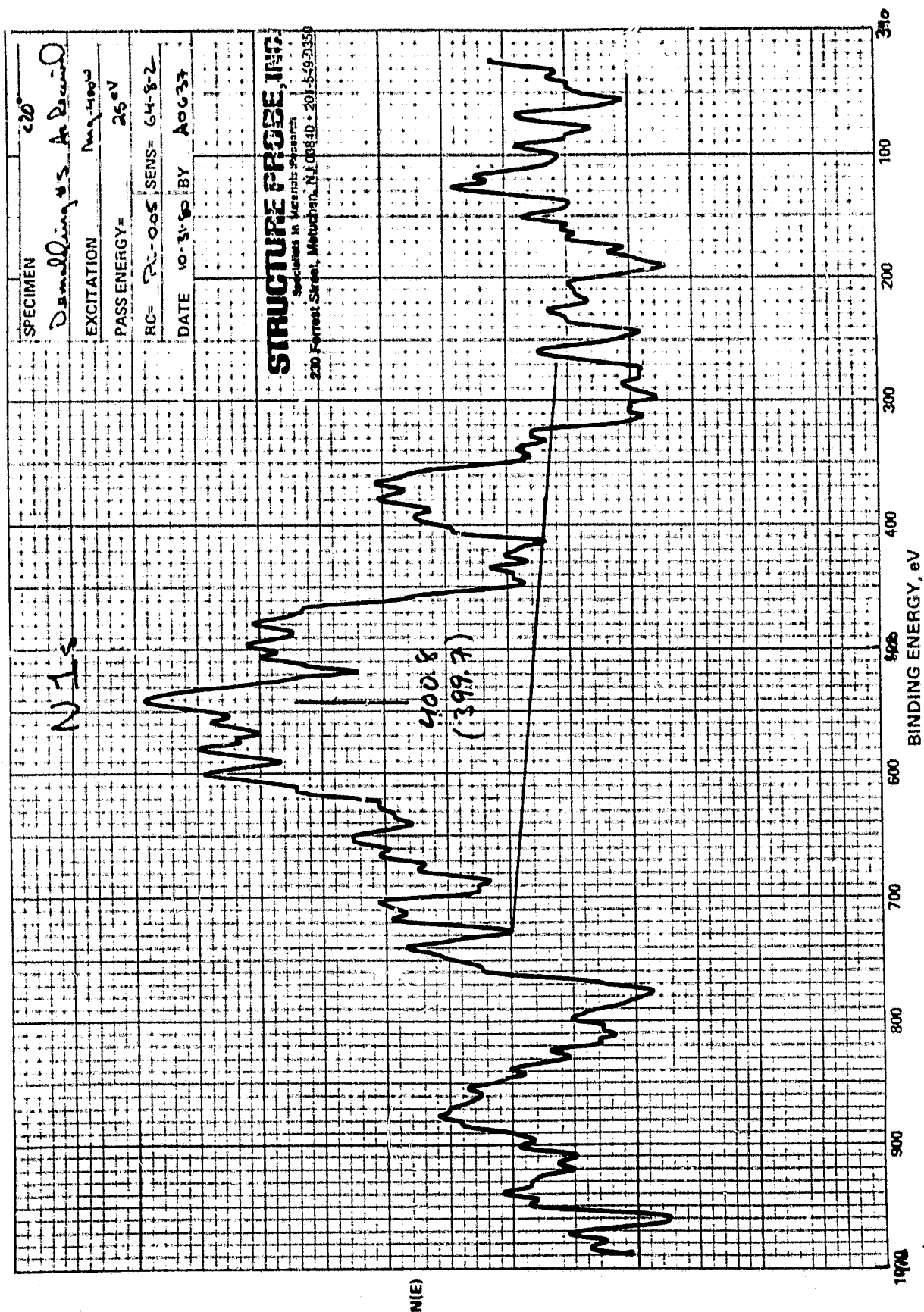
ORIGINAL FACE IS
OF POOR QUALITY


Figure 52

A-6393



PHYSICAL ELECTRONICS INDUSTRIES, INC.
174020

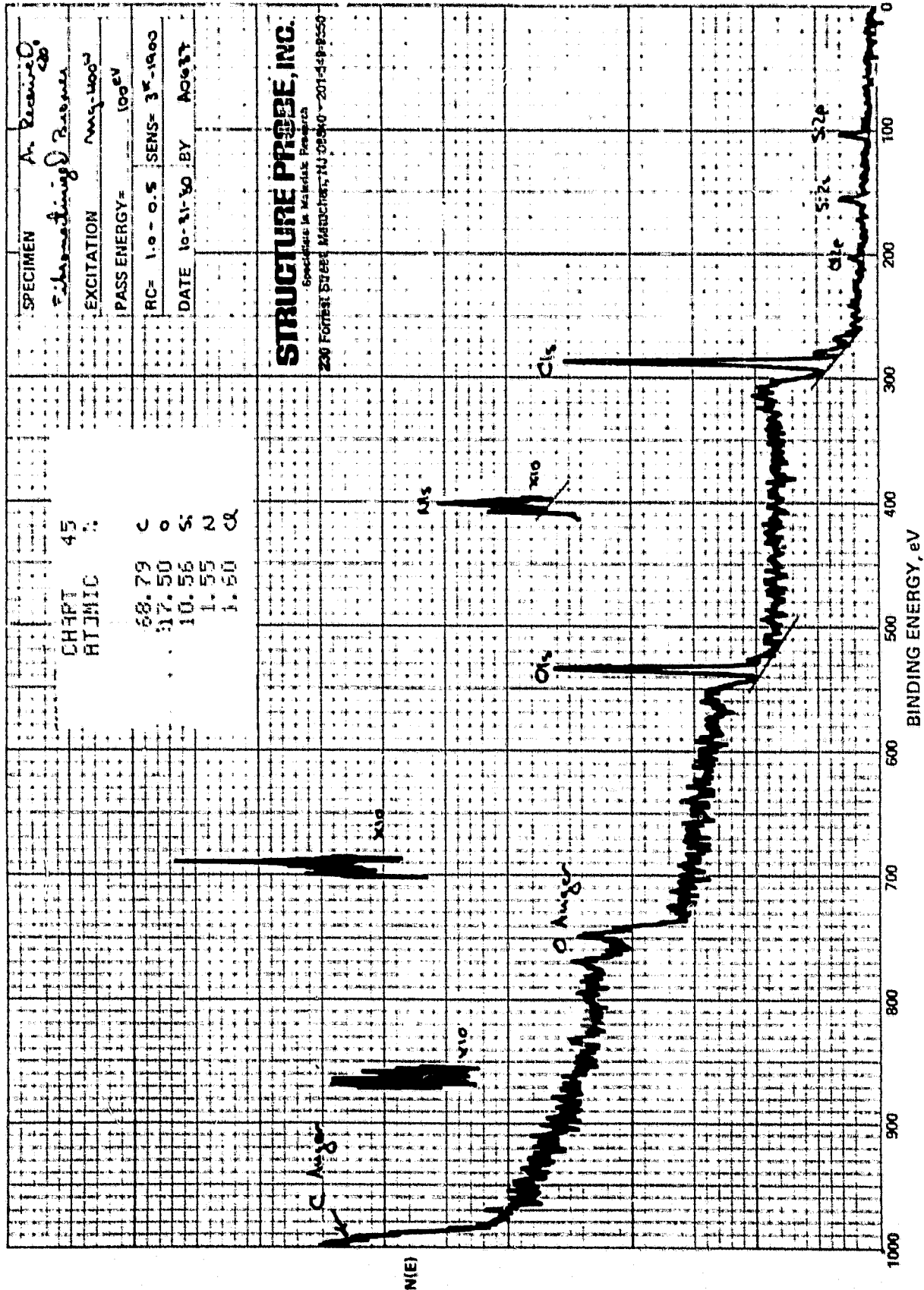


Figure 53

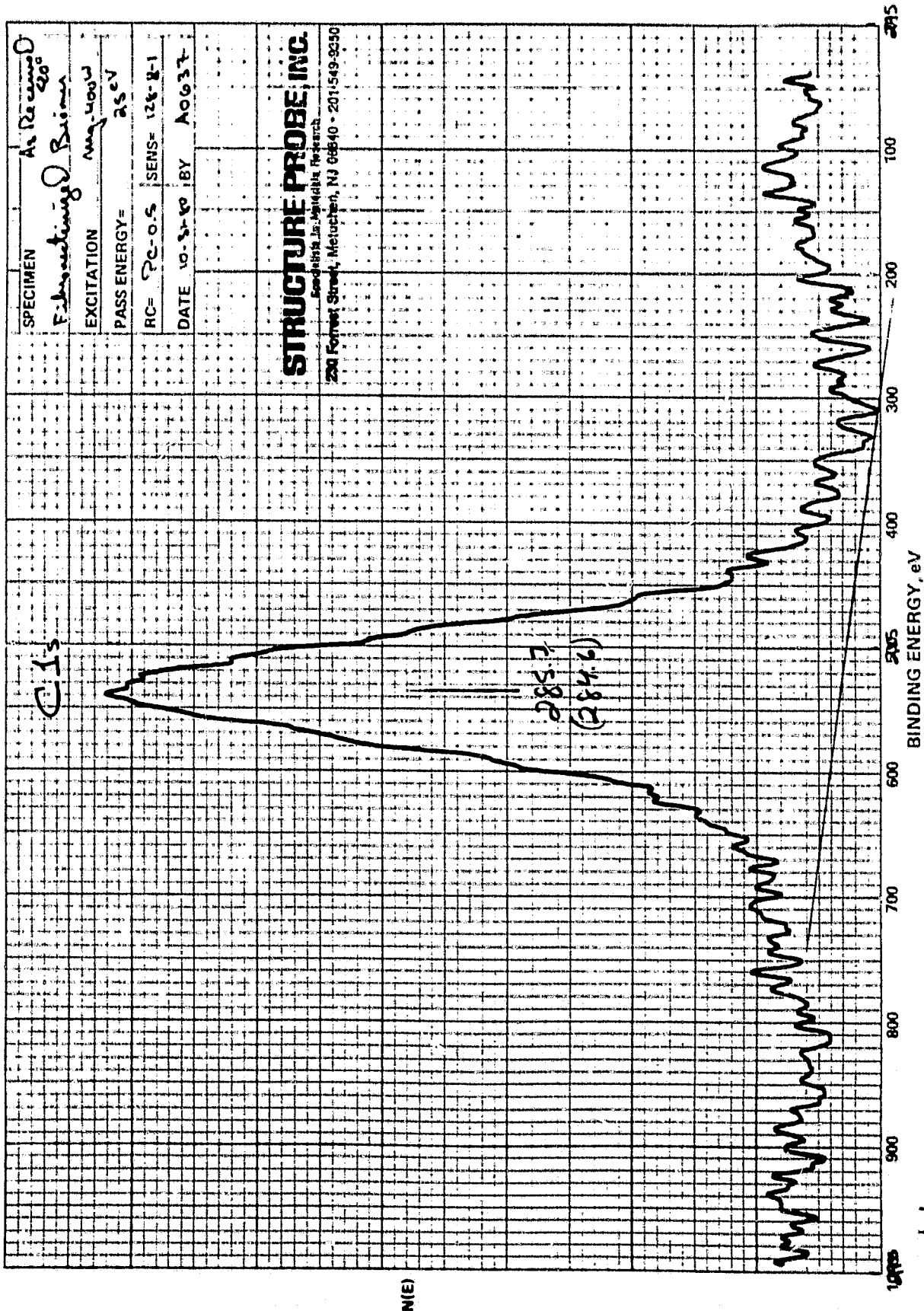


Figure 54

ORIGINAL PAGE IS
OF POOR QUALITY

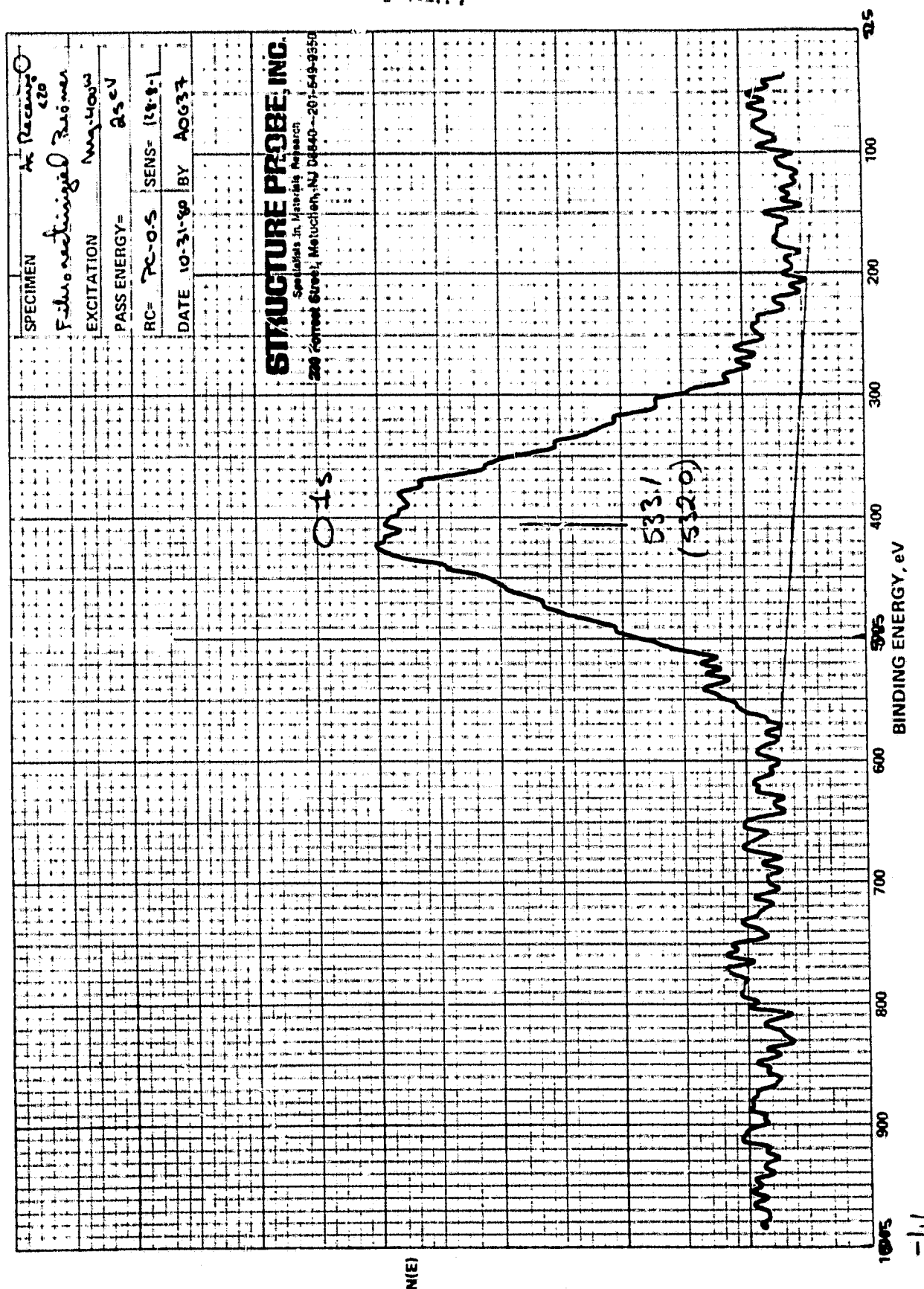


Figure 55

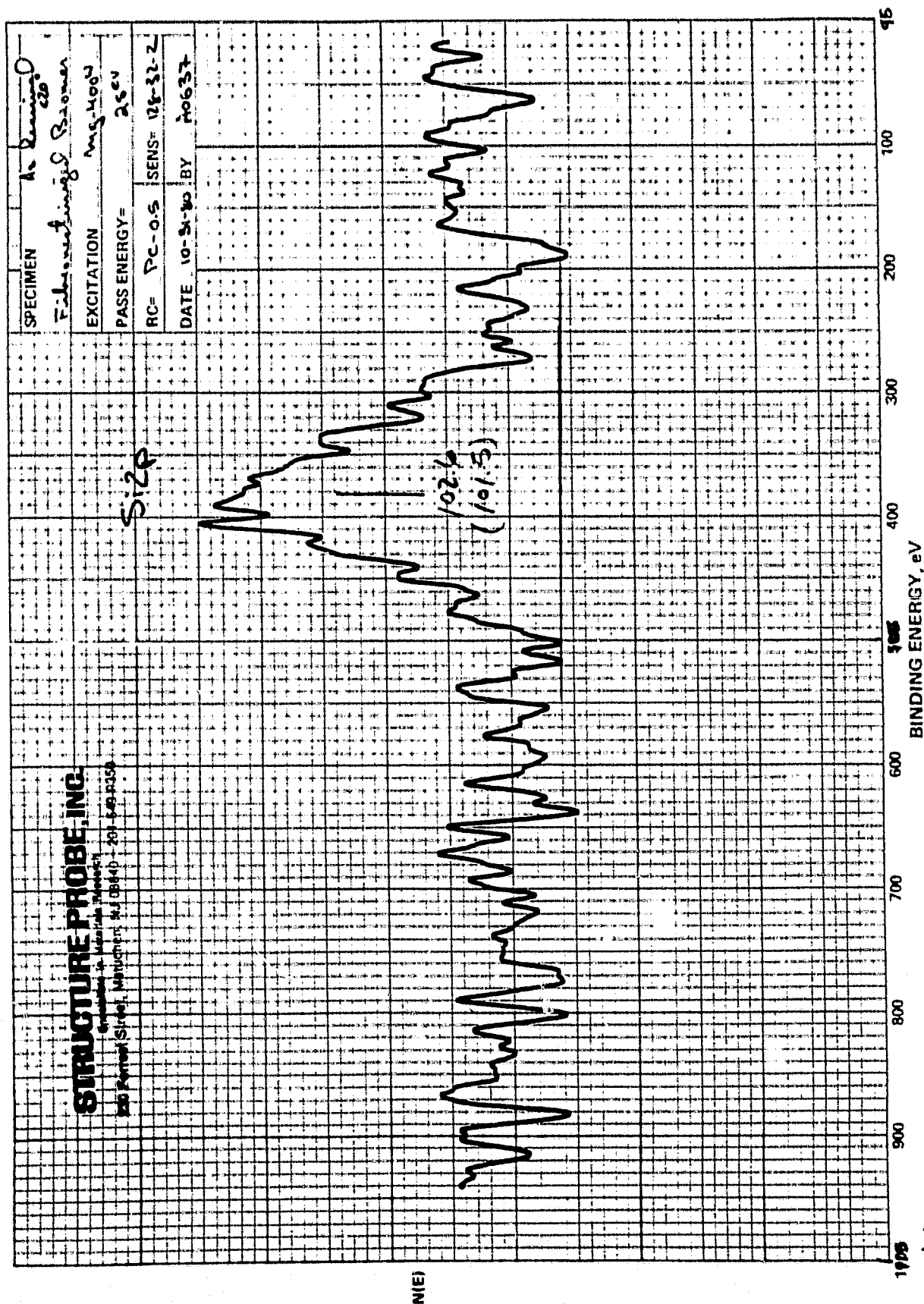


Figure 56

ORIGINAL PAGE IS
OF POOR QUALITY

6. ULTRASTRUCTURAL CHARACTERIZATION OF ION-SPUTTERED INTERFACES

Having established that Biomer aortic grafts and bladders could be produced essentially free of impurities originating from the sputtering process, we next proceeded to ultrastructurally characterize the blood interface.

Biomer grafts and bladders fabricated from ion-sputtered PTFE mandrels were cut into specimens 10 mm x 10 mm, and the negative-replica microtextured surface observed in the scanning electron microscope. Figure 57 is a low power overall view of the microtextured surface, featuring a symmetrical array of pillars. These pillars represent the holes originally formed on the PTFE mandrel during the mesh-screened ion-sputtering process. Pillars represent the negative replica of these holes, obtained when the textured mandrels were repeatedly immersed in Biomer solutions used to fabricate the grafts and bladders.

Figure 58 is another view of the microtextured blood-contacting surface of a typical Biomer bladder. In this higher magnification, the remarkable symmetry and reproducibility of the pillars is striking. Each pillar is 20 μm x 25 μm at the base, and approximately 40 μm in height.

At higher magnification (1000x), seen in Figure 59, the smallest surface details are clearly visible. It can be seen that the floor between pillars is not smooth, having instead a microtextured appearance. The reason for this wrinkled appearance is that we subjected the PTFE to an ion-sputtering "cleaning step." Following the initial ion-sputtering process using a nickel-photo formed mesh, the nickel mesh was manually removed, and the mandrel subjected to an additional round of surface sputtering, to clean the surface from most nickel and decomposition products emanating from the sputtering process.

Texturing of the polymer occurs by a collision process. Accelerated ions fragment atoms or parts of molecules from the polymer. Hard to etch

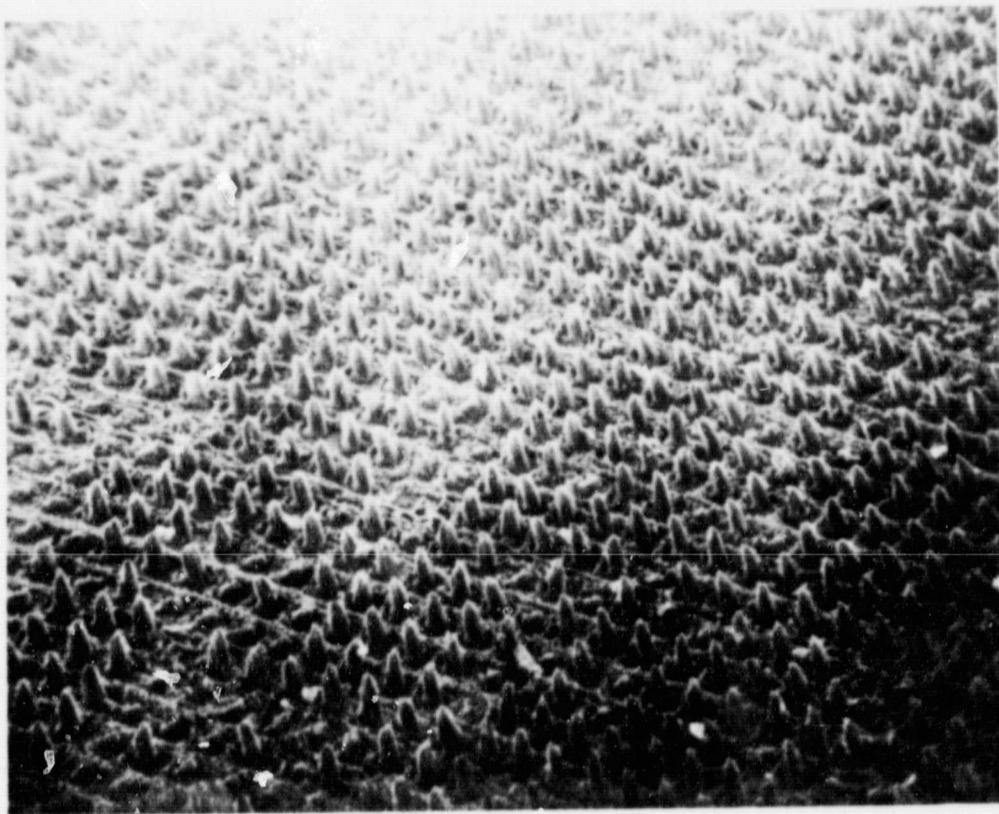


Figure 57. Low power view of NASA surface. (100x)

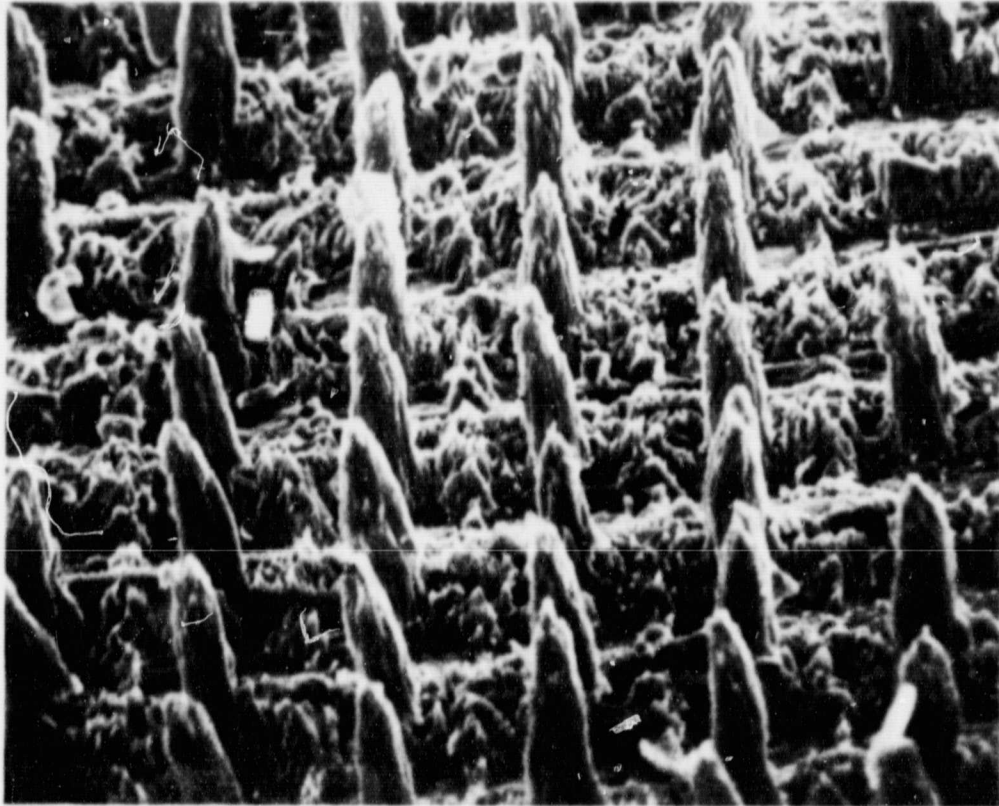


Figure 58. Scanning micrograph of NASA surface showing the remarkable symmetry of this blood interface. (400x)

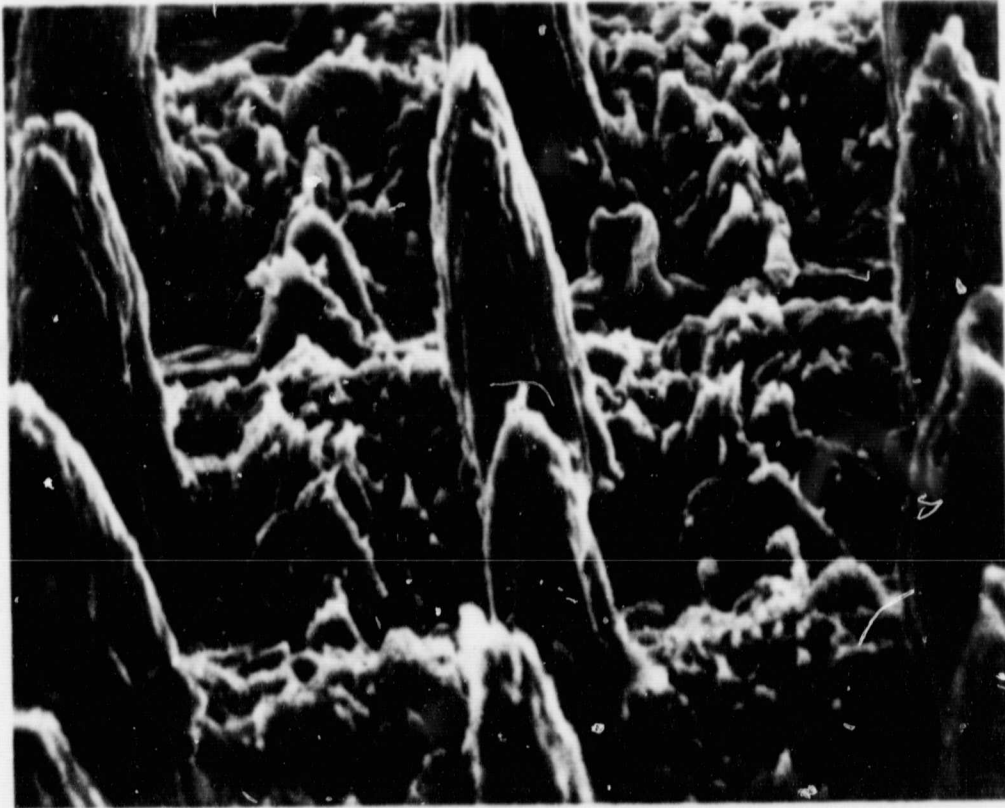


Figure 59. High power view of NASA surface. Each pillar shows a characteristic microtexture, derived from the sputtering process. (1000x)

molecular species are left standing; those easier to sputter are removed. Polymers such as PTFE behave in this fashion because they are inhomogeneous, having both amorphous and crystalline regions which sputter at different rates. The result is a wrinkled appearance on the surface, as shown in Figure 59.

The use of such a microtextured surface was expected to help in better anchoring a pseudoneointimal lining to the underlying polymeric substrate, and perhaps, improve long-term device performance.

7. IN VIVO STUDIES

Our protocol for in vivo studies was functionally divided into two parts: 1) implantation of aortic grafts and 2) implantation of Model 11S LVAD's. In all cases, the prostheses consisted of Biomer polyurethane, fabricated from ion-sputtered PTFE mandrels.

It was our original intent to evaluate two mat thicknesses, namely 40 μm and 75 μm ; unfortunately we only received from NASA-Lewis mandrels containing pockets 40- μm deep. We were informed by NASA that PTFE mandrels with pockets 75- μm deep could be available after the program termination date, and thus we were forced to perform all our studies with only one mat thickness.

We thus proceeded to evaluate in calves aortic grafts and Model 11S LVAD's. Our studies of ion-sputtered textured blood interfaces were all conducted with preseeded fetal fibroblasts. Results from program NO1-11V-3-2915 strongly indicated that preseeding prostheses with cultured fetal fibroblasts significantly increases the PNI adhesion to the Biomer. Summary data from these experiments are shown in the following table.

COMPARISON OF NEOINTIMAL ADHESION LEVELS
BETWEEN SEEDED AND NONSEEDED BLADDERS

Calf No.	Bladder Description	Duration (days)	Adherence (g/cm)
552	Integrally Textured Nonseeded	14	21
553	Integrally Textured Nonseeded	23	20
566	Integrally Textured Nonseeded	60	30
556	Integrally Textured Seeded	72	>500
559	Integrally Textured Seeded	30	>500

Good pseudoneointimal adhesion to the Biomer substrate is considered a crucial parameter, since poor adhesion results in delamination during prolonged flexing, with an increased risk of lining rupture and embolization. Preseeding the prostheses with cultured fetal fibroblasts results in highly collagenous biological linings that display greater adhesion to the polymeric substrate. With this experience in mind we decided to preseed all ion-sputtered prostheses with cultured fetal fibroblasts, in an effort to obtain the best possible adherence of the PNI to Biomer.

We are also aware that good PNI adhesion to integrally textured surfaces is largely due to mechanical entrapment of the biologic lining within the microfibrils which compose the surface. Adhesion is not entirely due to the presence of collagen; instead it is dependent on the entanglement of the lining into the natural undercuts provided by the microfibrils. Collagen being substantially stronger than fibrin contributes to the enhanced adhesion by providing a biologic lining with greater tensile and tear strength.

The mechanical entanglement provided by a conventional integrally textured surface is absent in ion-sputtered surfaces. Ion-sputtered surfaces are composed of symmetrical rows of mutually parallel pillars; this arrangement does not provide a natural anchoring mechanism for the PNI. In addition, this surface is not conducive to good attachment by fibroblasts. Preseeded fetal fibroblasts must attach well to the prosthesis prior to implantation to survive the initial shear of circulating blood in the first few minutes postimplantation. Otherwise they are dislodged by the rushing blood, with a subsequent weakening of the lining due to reduced collagen contents.

We thus decided to use fibronectins in some of our studies. Fibronectins are known to enhance adhesion of many cells (including fibroblasts) to a variety of polymeric substrates. We reasoned that passively adsorbing

fibronectins onto the ion-sputtered Biomer surfaces would increase fibroblastic adhesion, thereby resulting in a more collagenous, i.e., stronger and better attached, biologic lining.

With these considerations in mind, our in vivo protocol was as follows:

- Aortic Grafts
 - Implant two aortic grafts, fabricated from ion-sputtered cylindrical PTFE mandrels, 40- μ m deep. Surfaces preadsorbed with fibronectins, and preseeded with fetal fibroblasts. Nominal implantation duration: 2 months.
 - Gross examination:
 - a. Surface morphology
 - b. Continuity of PNI deposition
 - PNI Characterization
 - a. Quantitative determination of PNI adhesion
 - b. Thickness profiles of thin sections
 - c. Cytochemical PNI composition
- Model 11S LVAD's
 - Implant four LVAD's, fabricated from ion-sputtered PTFE mandrels, 40- μ m deep. Two LVAD's implanted untreated, and two pretreated with fibronectins. In all cases, surfaces to be preseeded with fetal fibroblasts. Nominal implantation duration: 1 month.
 - Gross examination
 - a. Surface Morphology
 - b. Continuity of PNI deposition
 - c. Examination of valves
 - PNI Characterization
 - a. PNI adherence levels
 - b. Thickness profiles
 - c. Cytochemical analyses

8. IN VIVO RESULTS

Two Biomer aortic grafts fabricated from ion-textured mandrels were implanted on 11/5/80 and 11/7/80, respectively. These studies were identified as NASA No. 1 and NASA No. 2.

NASA No. 1 was a 10.0-cm graft with a 20-mm internal diameter, ethylene oxide sterilized, and pretreated with $5 \mu\text{g}/\text{cm}^2$ of fibronectin preoperatively and seeded with fibroblasts. The graft was implanted in the descending thoracic aorta below the left subclavian artery in an end-to-end fashion. The animal did well postoperatively and was sacrificed on 1/15/81 after 71 days of survival. Autopsy examination revealed that a lining within the polyurethane graft had separated from the underlying graft surface. There was a tubular lining (unattached except at the proximal and distal ends) consisting of endothelium and a grayish white pseudointima in the central area. The endothelium had grown from the intima of the aorta at the proximal and distal anastomoses.

This was a good lining but unfortunately was not attached to the underlying graft surface. This is shown in Figure 60. This photograph is an overall view of the aortic graft immediately after animal sacrifice. The graft has been sectioned in half, and the sides reflected downward to expose the resulting pseudoneointimal lining.

The lining was strong, thin, and glistening, but displayed very poor adhesion. In fact, the adherence was so poor the lining spontaneously delaminated from the Biomer substrate during manipulation.

Histologically, the lining consisted of a highly cellular matrix; fibrin was observed near the Biomer substrate, with a more collagenous portion toward the liminal surface. The poor adhesion was due to the fibrin layer, which is mechanically weak and easily ruptured. Figures 61 thru 63 are representative histological sections of this lining, showing the cellularity of the PNI.

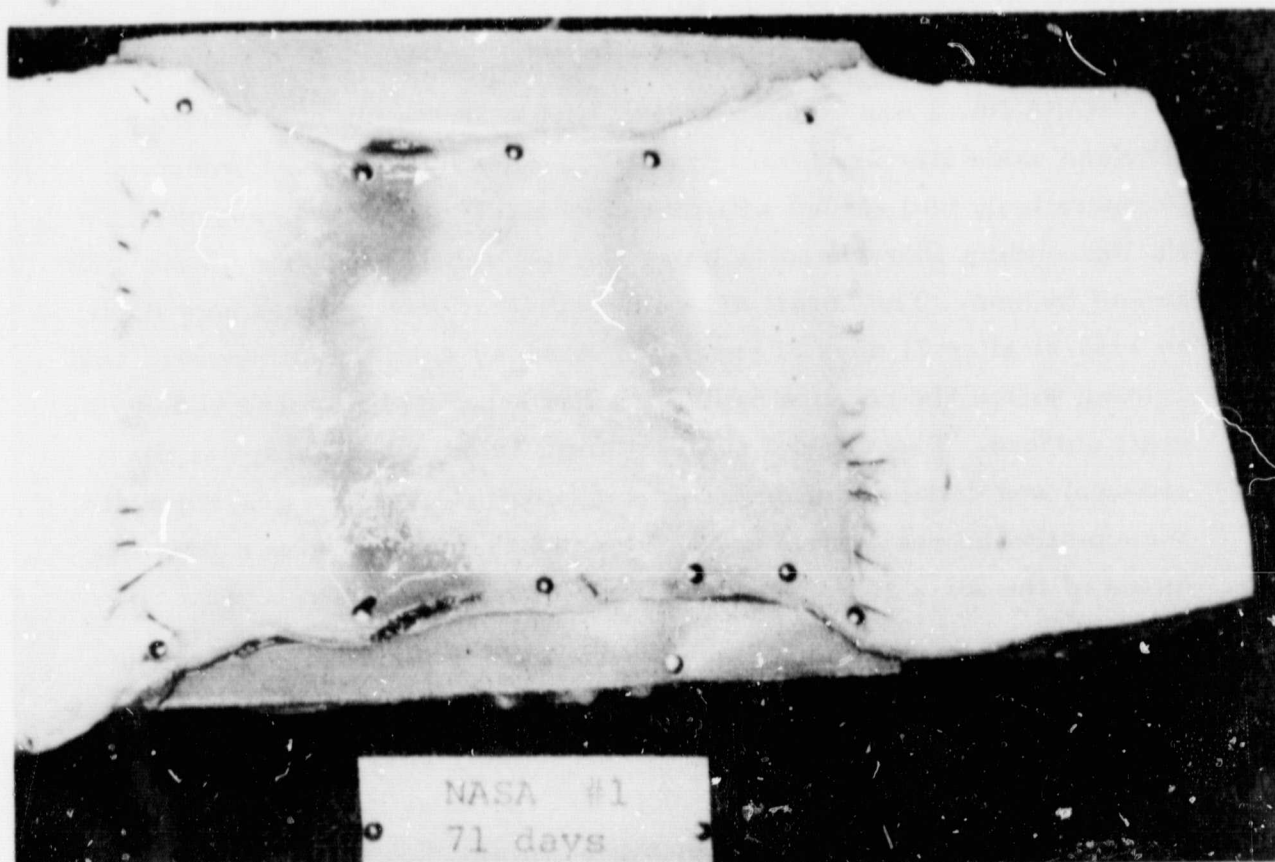


Figure 60. Gross view of PNI from NASA No. 1 graft.
The lining was thin and smooth, but poorly attached.

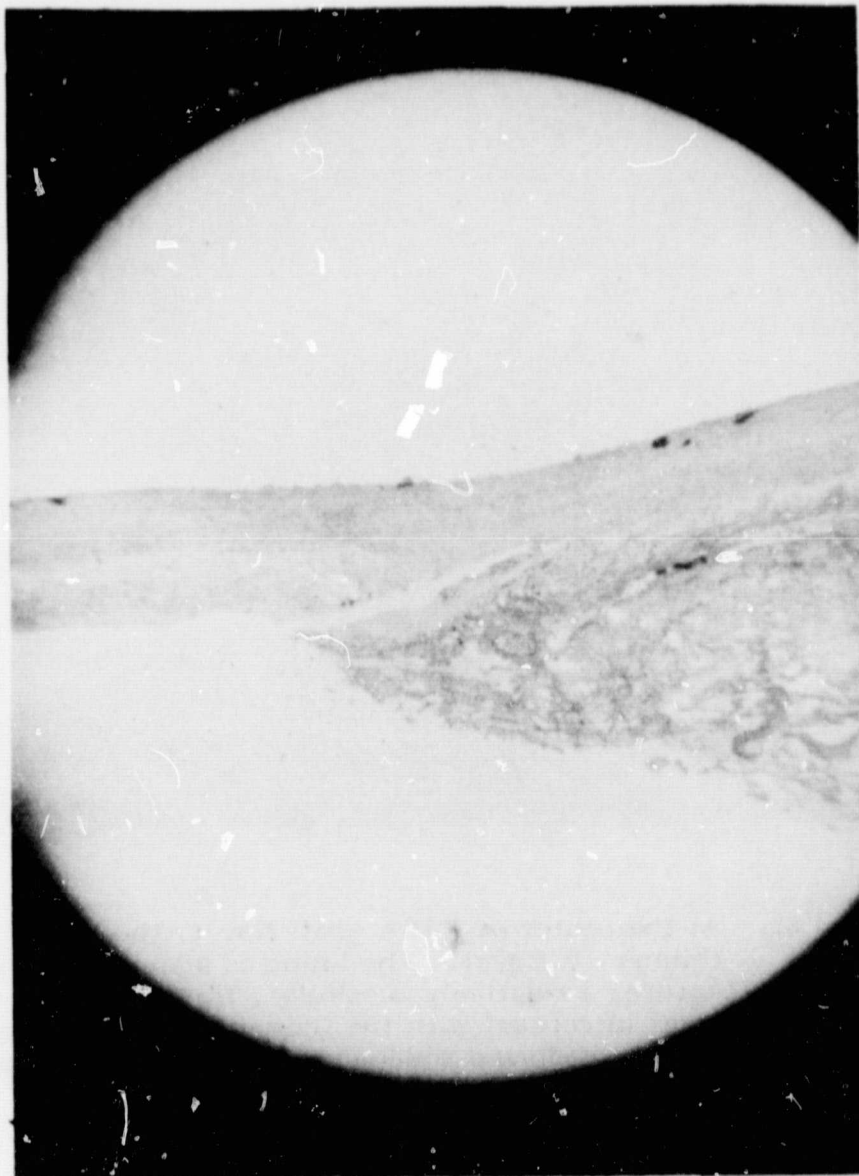


Figure 61. Low power section of NASA No. 1 graft at the anastomosis site. The aorta is seen as a relatively thin lining; the graft PNI is composed of a thick fibrin lining, overlaid with a highly cellular, collagenous layer.

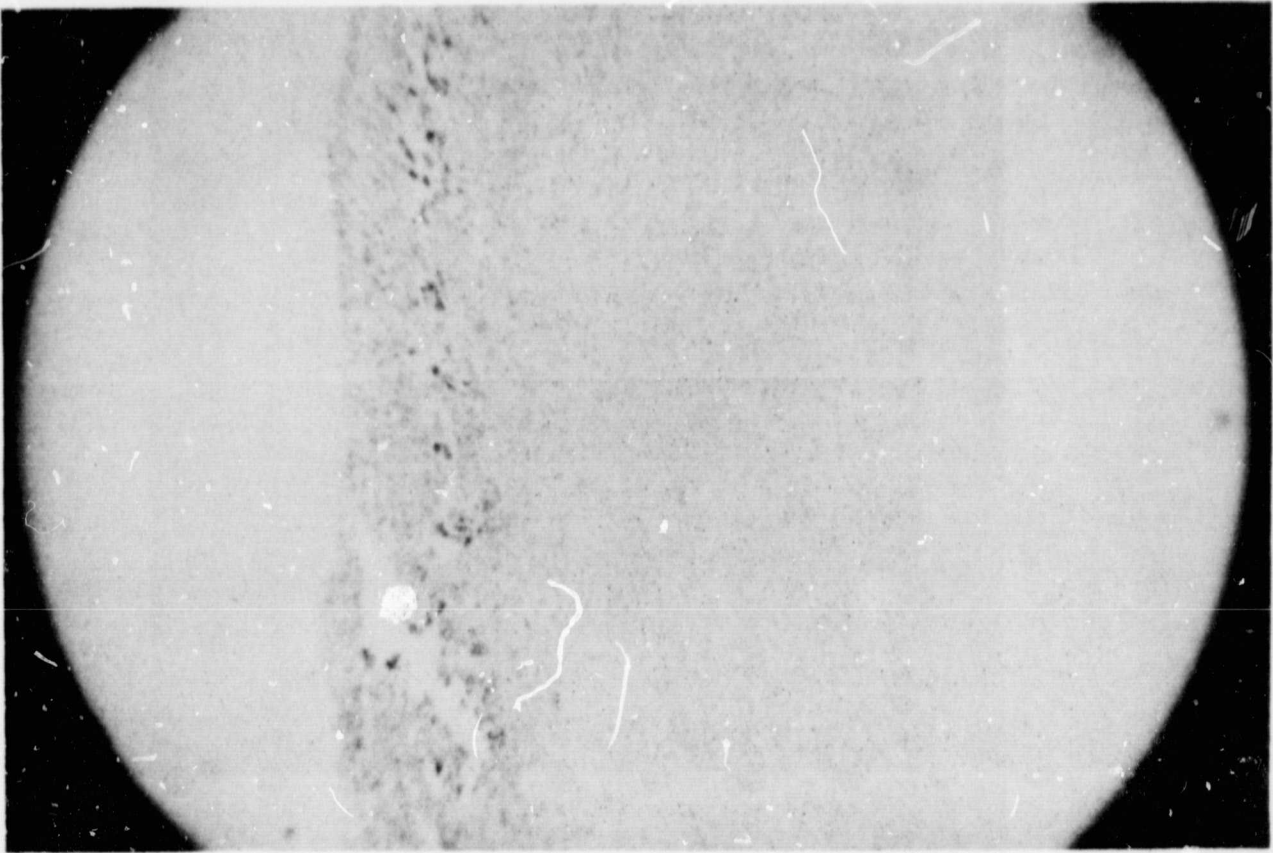


Figure 62. At the center of NASA graft No. 1, the lining is much thinner (0.8 mm). The lining is again bilaminar in nature; a relatively acellular, fibrinous, and edematous layer in contact with the Biomer, and a stronger, more highly organized collagenous layer towards the luminal surface

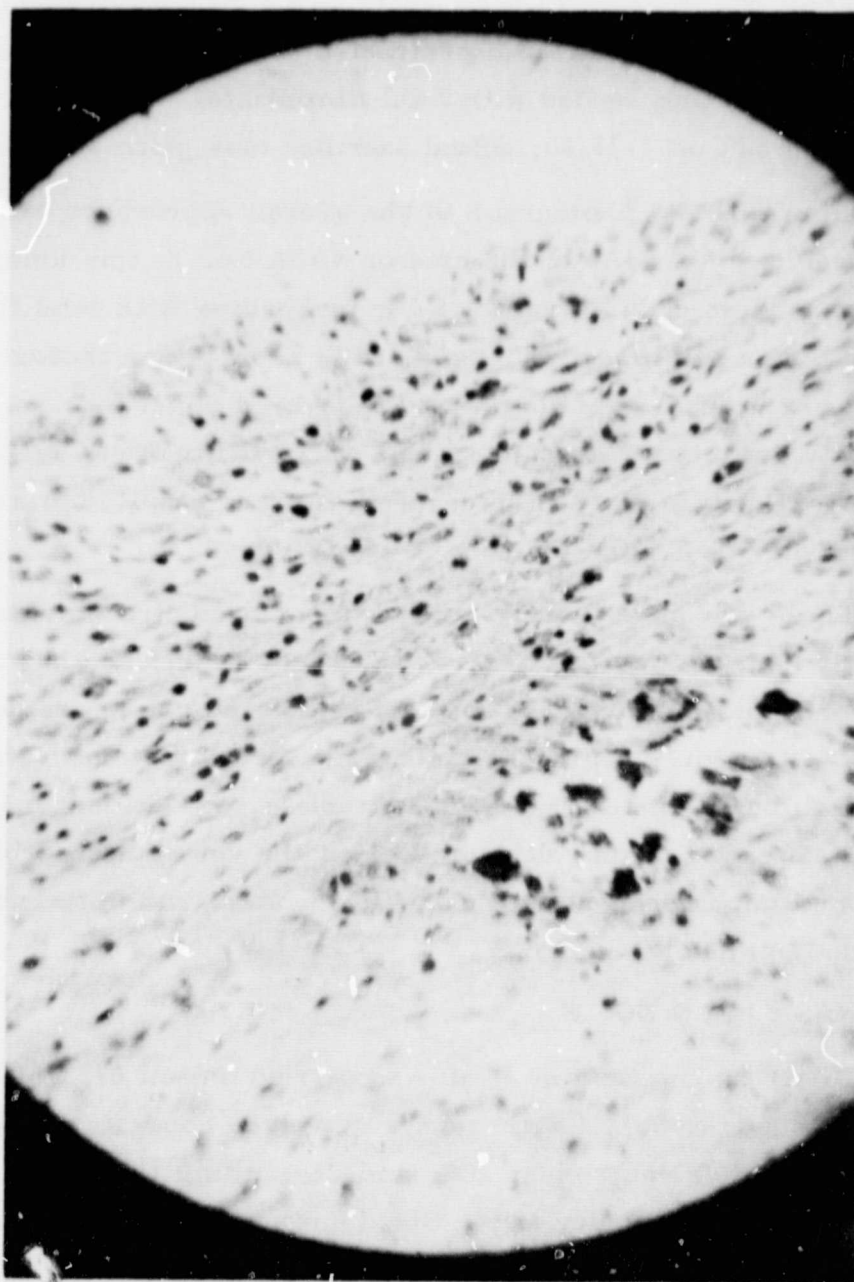


Figure 63. High power micrograph at the fibrinous layer of NASA No. 1. The layer is highly edematous, filled with leukocytes, and fractured in many places. One representative fracture is shown calcified and filled with edematous fluid.

NASA No. 2 was a 10.0-cm graft with a 20-mm internal diameter, ethylene oxide sterilized, and pretreated with $5 \mu\text{g}/\text{cm}^2$ of fibronectin preoperatively and seeded with fetal fibroblasts. The graft was implanted in a 90-kg calf on 11/7/80; animal sacrifice took place on 1/22/81.

Figure 64 is a photograph of the overall appearance of the graft at animal sacrifice. As in the case of NASA No. 1, this lining was also very poorly attached, in spite of our preseeding with fetal fibroblasts, and the use of fibronectin. Figure 65 is a low power micrograph at the center of the graft, showing a typical layered appearance. A thin layer of poorly organized, edematous, and calcified fibrin can be seen adjacent to the textured Biomer. This layered lining is easily ruptured, accounting for the very poor adhesion seen in this study.

These preliminary aortic graft studies predicted troublesome post-operative periods for the LVAD's. Years of experience has taught us that aortic graft studies are simplest, since the grafts are non-flexing; the LVAD bladders represent the most severe condition in the development of non-thrombogenic surfaces. Nonetheless, we decided to go ahead with our LVAD experiments, although we felt the ion-sputtered blood interfaces had not undergone sufficient development and optimization for the intended application.

8.1 NASA LVAD NO. 2

LVAD implantation in a calf was carried out on 6/23/81 using bladder No. 397. The model XI with xenograft valved conduits was interposed between the left ventricular apex and descending thoracic aorta at the left of the 8th rib posteriorly. Bladder was treated with fibronectin and seeded with fibroblasts prior to implantation in the calf.

Elective sacrifice of this animal was carried out on 7/22/81. The pump bladder contained scattered areas of poorly attached fibrin and other areas where there did not appear to be any biologic material present

ORIGINAL PAGE
BLACK AND WHITE PHOTOGRAPH



Figure 64. Overall appearance of NASA No. 2 graft at sacrifice. The PNI was thin and strong, but very poorly attached to the Biomer substrate.

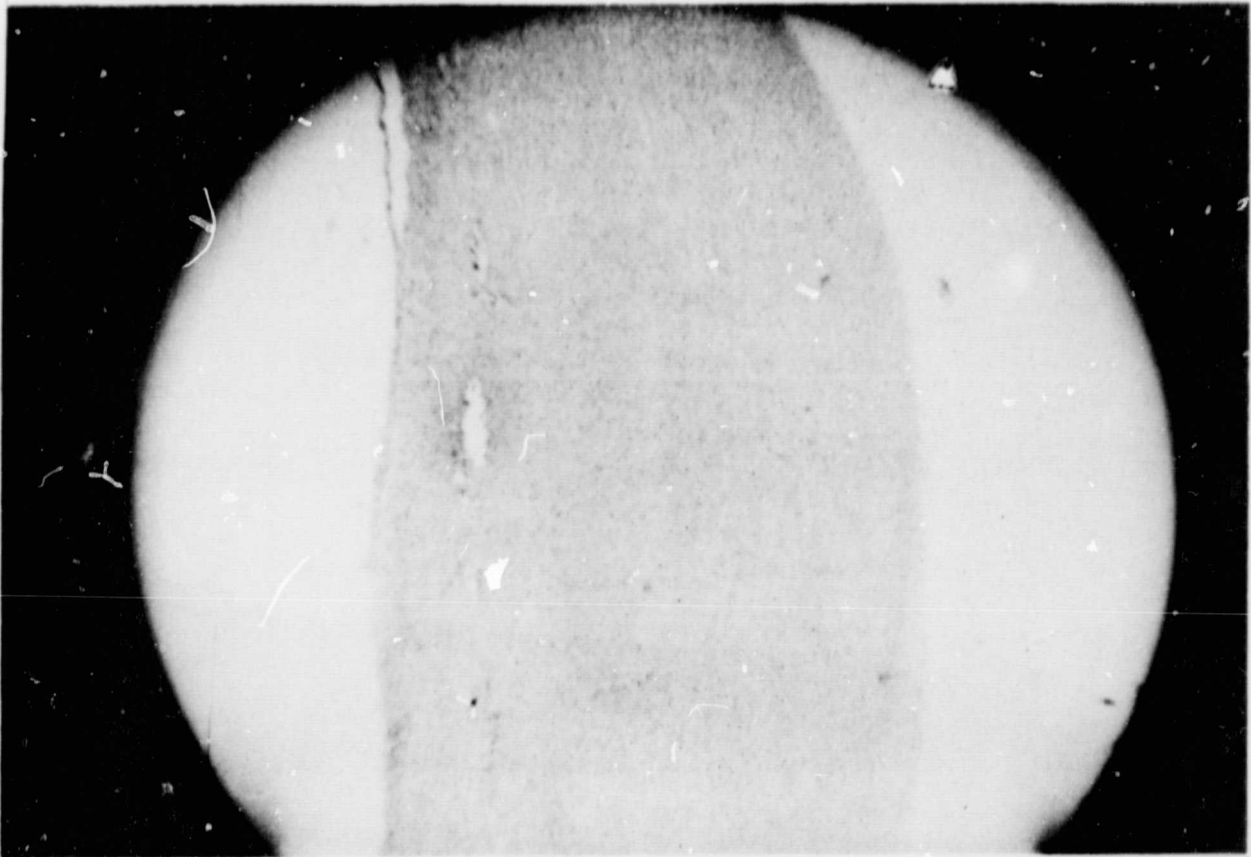


Figure 65. Low power view of the lining at the geometric center of the NASA No. 2 graft. The lining is composed of two distinct layers: adventitial layer of loose, edematous, and calcified fibrin, and a luminal layer of organized collagen containing many elongated cells.

at all. There was no evidence of clot in the inflow or outflow elbows and the valved conduits were also free of thrombus. Examination of the liver, kidneys, lungs, GI tract, and heart revealed no embolic damage. In summary, there was very little biologic material present on this pump bladder surface but scattered areas of loose thrombus occupied a small amount (25 percent) of the blood-contacting area.

8.2 NASA LVAD NO. 3

LVAD implantation was carried out in this animal on 7/23/81 using bladder No. 399. The surface of the bladder was seeded with fibroblasts. The animal developed an acute abdominal distress with distension on 7/27/81 and was sacrificed.

Four LVAD's were studied, two pretreated with fibronectins, and two implanted without any surface pretreatments to serve as controls. In all cases the bladders were seeded with fetal fibroblasts; then studies were designated as NASA calves 1 to 4, respectively. Examination of the pump bladder revealed partial obstruction of the outflow end of the device with a large amount of thrombus that apparently had separated from the bladder surface. The thrombus accumulation had extended to the xenograft outflow valve. Examination of the heart, liver, and lungs was unremarkable. Sectioning of the kidneys revealed diffuse embolic damage with multiple cortical infarcts. Examination of the gastrointestinal tract also revealed extensive embolic damage. Summary: This animal died of diffuse systemic embolization that developed from the pump bladder surface. The fibrin-cellular lining had completely separated and fragmented.

8.3 NASA LVAD NO. 1

A Model XI penumatic LVAD was implanted in this animal on 6/16/81. The bladder was No. 395 and this textured surface was treated with fibronectin and seeded with fibroblasts. The pump was interposed between the left ventricular apex and descending thoracic aorta. The animal was sacrificed on 6/30/81 because of an outflow pump obstruction which diminished

pump output. Post mortem examination revealed detachment of the developing lining which had formed an obstructive mass of fibrin and cells which occluded 75 percent of the outflow metal elbow of the device. An accumulation of thrombus extended from this area to the outflow xenograft valve within the outflow conduit. Examination of the heart, liver, lungs, kidneys, and GI tract revealed no evidence of embolic damage or hemorrhage. The animal was sacrificed before embolic episodes could occur. The major problem with this study was separation of the lining from the bladder surface. Figure 66 presents the histological findings from this study.

8.4 NASA LVAD NO. 4

LVAD implantation was carried out on 9/3/81 with pump bladder No. 407. The bladder surface was seeded with fibroblasts in this experiment. The animal pumped satisfactorily for 2 weeks and then developed evidence of LVAD obstruction and embolic organ damage. The animal was sacrificed on 9/20/81 after 17 days of assisted circulation. Autopsy examination revealed separation of loose thrombus from the pump bladder surface with fragmentation of clot. There was extensive organ embolization involving the kidneys and gastrointestinal tract. Summary: There was poor attachment of a developing fibrin layer to the pump bladder surface which led to separation and embolization.

ORIGINAL PAGE
BLACK AND WHITE PHOTOGRAPH

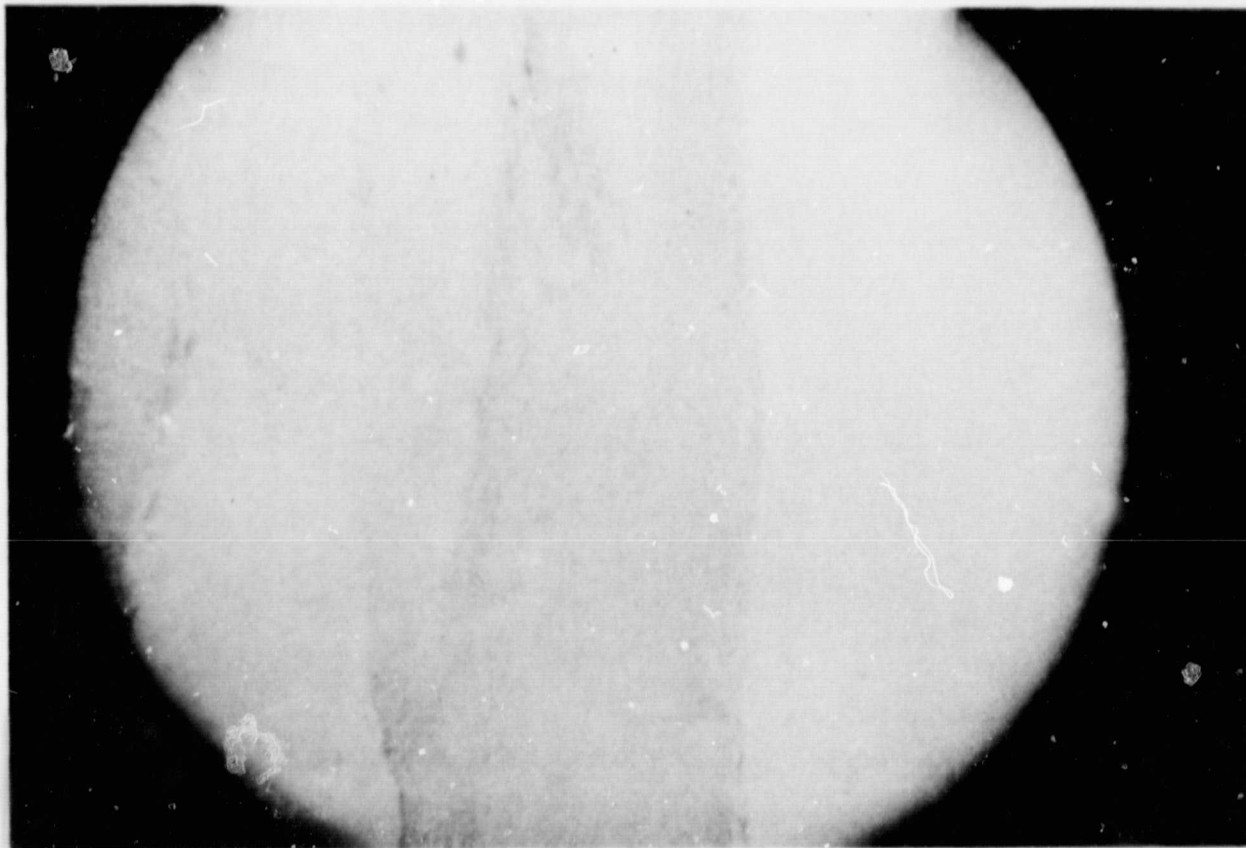


Figure 66. Overall histological view of the PNI from NASA LVAD No. 1. The lining was thin, but delaminated from the bladder, causing flow obstruction. Loose, edematous fibrin can be observed in the lining closest to the bladder.

9. DISCUSSION

Our basic postulate in the study of aortic grafts and LVAD bladders fabricated from ion-sputtered PTFE mandrels was that a reduced mat thickness would result in a correspondingly decreased PNI thickness. Our observations demonstrate the feasibility of this approach.

The following table summarizes our findings.

PSEUDONEOINTIMAL LININGS THICKNESS

	Integrally Textured (0.31 mm)	Ion Sputtered (25 x 25 x 40 μ m)
Grafts	1 mm	0.8 mm
LVAD's	0.8 mm to 1.2 mm	0.7 to 1.1 mm

While a reduced mat thickness is considered advantageous in chronically flexing devices such as ventricular bypass prostheses, adhesion of the biologic lining to the underlying substrate is another crucial requirement. As demonstrated in our LVAD experiments, a poorly attached PNI will eventually result in thromboembolic complications.

The use of fibronectin increased lining adhesion, but not enough to provide trouble-free implantations. Fibronectin enhances fibroblastic adhesion to Biomer; the more firmly attached fibroblasts are more capable of surviving the initial high shear generated by the circulating blood. A greater number of attached fibroblasts, in turn, result in a stronger, more collagenous PNI.

We conclude that ion-sputtered surfaces, as presently constituted, are unsuitable as chronic, non-thromboembolic surfaces. Perhaps the use of higher pillars (25 x 25 x 75 μ m) would improve adhesion, due to the increase in available surface area.

The use of higher pillars falls within the category of surface optimization. This preliminary program could only study one mat thickness because only one ion-sputtered mandrel was received from NASA. Ion-sputtered surfaces merit a more detailed and comprehensive investigation; we thus recommend that additional studies be carried out to optimize ion-textured surfaces designed for use in blood-contacting prostheses.

END

DATE

JUL. 21, 1982